REPORT AND RECOMMENDATIONS ON MALARIA :

A SUMMARY

International Cooperation Administration
Expert Panel on Malaria

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INTERNATIONAL COOPERATION ADMINISTRATION EXPERT PANEL ON MALARIA†

Late in 1959, it became apparent that an independent appraisal of the status and prospects of the rapidly expanding global program for the eradication of malaria was needed to orient discussions of future United States participation. In December, the International Cooperation Administration (ICA) named a panel of twelve American experts to consider the future position of the United States with respect to malaria eradication. The ICA Expert Panel on Malaria met on four occasions between the first week in January and the last of April 1960.

At the opening session, Dr. Eugene P. Campbell, Director of the Office of Public Health, ICA, welcomed the Panel, and outlined the Panel's terms of reference. They were to (1) assess the progress of world-wide malaria eradication and consider the future position of the United States on malaria eradication; (2) estimate future program requirements in time, personnel, commodities and research and predict the future of malaria eradication; (3) review the over-all financial situation, estimate future costs and advise on how to induce other countries to contribute to these costs; (4) examine and advise on special epidemiological features, summarize technical problems and provide sound orientation; (5) assess ICA relationship to malaria eradication and advise on ICA administrative problems; and (6) advise how malaria eradication in Africa can be undertaken effectively.

The Panel's report, submitted in August 1960, is here summarized in sections as follows:

1. Historical Background
2. International Malaria Eradication
3. Progress in Malaria Eradication
4. Technical Considerations
5. Organization and Administration
6. Cost of Global Eradication
7. Evaluation and Measurement of Disappearing Malaria
8. Malaria Eradication and Political Problems
9. International Responsibility in Malaria Eradication
10. Tropical Africa
11. Social Implications of Malaria Eradication
12. Findings and Recommendations

Annex I: Countries with ICA Malaria Eradication Projects

Annex II: Examples of Malaria Eradication

* This report contains the collective views of a group of experts and does not necessarily represent the decisions or the stated policy of the International Cooperation Administration.

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1. HISTORICAL BACKGROUND

In 1880, a French army doctor, Laveran, in Algeria, discovered in a patient's blood the para-

site that causes malaria. In 1898–99, Ronald Ross, in India, and Grassi, Bignami and Bastianelli, in Italy, proved experimentally that the malaria parasite is transmitted from person to person by mosquitoes. Moreover, Ross and the Italians made it clear that the malaria parasite is not simply carried from one person to another, but that the malaria parasite must go through an essential developmental period of ten days or more in the body of the insect before the mosquito can transmit it. It was quickly demonstrated that the parasite could develop only in mosquitos of a single genus, *Anopheles*. Gradually, it became clear that only certain species of *Anopheles* feed on man often enough to be effective carriers of malaria. It was found that these malaria mosquitoes have preferences as to the type of water in which they lay their eggs to develop into larvae and pupae. Some select marshes, others streams, puddles, lagoons, ponds, springs, and so on. The adults of some species were found to prefer indoor resting places in the daytime; others outdoor shelters. Most of the malaria-carrying species were found to feed at night inside human habitations. All of these and other fundamental facts of malaria were exposed during the first third of the twentieth century by the genius and patient studies of many men in many nations.

Attack on the Mosquito Vector

In view of these basic discoveries, the modern attack on malaria began with attempts to destroy the causative parasite in man and the transmitting insect in nature; the former by quinine, the latter principally by larviciding and drainage. Although Gorgas in Cuba, Watson in Malaya, Chagas in Brazil, and others, successfully attacked the malaria mosquito in the early years of the century, many scientists still doubted the economic feasibility of controlling mosquitos. So, for many years, there was widespread resistance to the use of anti-mosquito measures for malaria control.

Anti-larval. Gorgas and LePrince in the Panama Canal Zone, 1904–1914, the United States Public Health Service in Southeastern States, 1912 onwards, and The Rockefeller Foundation at home and abroad, 1916–1954, repeatedly demonstrated the effectiveness and economy of malaria control by anti-larval measures. The cumulative effect of these demonstrations led to the widespread practice of larviciding and drainage. This reduced the incidence of malaria, chiefly in urban communities, since cost was a deterrent in rural areas.

Anti-adult. In 1935, Park-Ross and de Meillon of the Public Health Service of South Africa reported success in controlling malaria at relatively low cost by attacking the adults of the malaria mosquito in their daytime resting places by systematic spraying with pyrethrum in kerosene. This novel method of malaria control, the efficacy of which was soon confirmed in India, pointed the way which has led to the present era of malaria eradication. Pyrethrum had no residual effect; thus frequent sprayings were necessary, but it proved to be more effective and cheaper in many areas than larviciding had been. For the first time in history, it became economically feasible to control malaria in parts of the rural tropics.

Species-eradication. In 1939–40, Soper and Wilson and their Brazilian colleagues adapted the administrative techniques developed some years previously for the species-eradication of the yellow fever mosquito, *Aedes aegypti*, to the eradication of *Anopheles gambiae* in northeast Brazil, where this dangerous African vector had established a bridgehead almost a decade earlier. Later (1944–45) these techniques were adapted to the eradication of *Anopheles gambiae* from Egypt, which had been invaded from the Sudan in 1942. These demonstrations of species-eradication of vector mosquitoes were valuable in validating the concept of eradication among malariologists.

Spontaneous Disappearance of Malaria Parasite

The eradication of *Anopheles gambiae* from Brazil led to the clear-cut observation of the rapidity of the dramatic fall in malaria rates produced by halting transmission and preventing new infections. *Anopheles gambiae*, introduced from Africa, had transformed low endemic malaria into a raging epidemic, killing many thousands, and producing among the survivors a parasite rate of over 65%. By the end of the first year of effective anti-mosquito work, the parasite rate had fallen to 9.8%; at the end of the second year, to 0.45%. This observation added materially to the evidence indicating that the human body terminates most malaria infections within three years, even in the absence of specific treatment, when reinfection is prevented. This is the basic

mechanism of the disappearance of malaria on which eradication is predicated.

Role of United States

The United States Public Health Service. The United States Public Health Service (USPHS) has been the most powerful force in the development, first of malaria control and then of eradication in this country. Beginning about 1912 it developed an educational program followed by malaria field studies and control demonstrations that made possible an extensive and successful anti-malaria program during the World War I period. Over 40 anti-mosquito projects in some 15 states protected one and three-quarters million civilians and some 800,000 military personnel. Many towns that benefited by this project continued the control measures after the war. Thanks to USPHS stimulation and help, malaria control programs were extended into more and more rural areas, especially after Paris green was shown to be effective as a larvicide in 1921.

During the depression years of the 1930's, many factors combined to promote endemic and even epidemic malaria. The Civil Works Administration, the Emergency Relief Administration and the Works Progress Administration, carried out numerous anti-malaria projects, stimulated and supervised by the USPHS.

Commencing in 1942, vigorous malaria control programs were initiated by the USPHS and the United States Armed Forces in and around training camps and cantonments in southern areas. No fewer than 2,200 anti-malaria projects were carried out in 24 states. This tremendous effort, added to the routine control programs in various counties, reduced malaria to a low level by the end of World War II. This led to the decision to undertake malaria eradication in the United States.

The concept of national malaria eradication had been born in the United States a generation before. The earliest statement was that of F. L. Hoffman who published in 1916 "A Plea for National Committee on the Eradication of Malaria" and, in 1917, "A Plea and a Plan for the Eradication of Malaria." These proposals were not immediately fruitful in promoting malaria eradication because available anti-malaria methods were not financially practicable. However, they did lead to the formation of the National Malaria Committee in 1916; it was from the work of this Committee that the seeds of eradication in the United States eventually germinated.

First United States bilateral programs—IIAA. The Institute of Inter-American Affairs (IIAA) was incorporated in 1942 by the United States Government, one of its purposes being co-operation with the American Republics in the solution of their urgent health programs. Malaria, the most urgent of these, was from the beginning given top priority. IIAA participated in malaria control projects in 17 of the 19 malarious Republics, with relative freedom from the bureaucratic restrictions under which national health services often labor. This participation was a prelude to expanded bilateral participation of the United States throughout the world in malaria control projects, and eventually in world-wide malaria eradication.

The Rockefeller Foundation. Another agency that had a powerful impact on malaria control and the development of the concept of eradication was The Rockefeller Foundation. From 1916 to 1954, the Foundation co-operated in malaria investigation, training, and control projects in 15 states at home and 45 countries and territories abroad. In its program it stimulated and aided research to elucidate general and local problems of malaria incidence and transmission; practical control demonstrations; training programs; and the establishment of national malaria services and offical organizations and institutes for malaria study and control. In this way the Foundation had an important part in laying foundations for the present remarkable acceleration in man's attack on malaria.

Notable in The Rockefeller Foundation effort was the species-eradication of *Anopheles gambiae* in Brazil and in Egypt already referred to.

Early Role of International Health Agencies

The League of Nations. The Health Section of the League of Nations was created in 1923; it set up in its first year a subcommittee that in 1924 became its Malaria Commission. This Commission developed considerable co-operation between nations in the exchange of information about malaria, in laboratory experiments, and in the training of personnel for malariology. The Commission did much to make clear how the epidemiology of malaria varies from place to place so that local studies are important in the planning of control. The League convened several important meet-

ings, including the Pan African Health Conferences in Johannesburg in 1935 at which Park-Ross reported the first successful malaria control by the pyrethrum spray-killing of adult malaria mosquitoes. All in all, the Malaria Commission of the Health Section of the League of Nations was highly influential in stimulating governments to pay attention to malaria and to think of malaria control as an international problem. Although the United States was not a member of the League of Nations, the co-operation of some of its leading malariologists was enlisted and financial assistance from The Rockefeller Foundation accepted by the Health Section.

The Pan American Sanitary Bureau. The Pan American Sanitary Bureau has had a profound influence on the development of malaria eradication in the Americas. The Bureau's first anti-malaria activities were chiefly collecting data, conducting surveys, stimulating anti-malaria projects and the training of personnel. A *Comisión Panamericana de Malaria* was set up in 1938–40, consisting of outstanding malariologists from the United States, Venezuela, Brazil and Argentina. The creation of the Pan American Health Organization in 1947 gave to the Bureau hemispheric coverage essential to malaria eradication.

Early DDT Periods

In 1939–40, Müller and colleagues in Switzerland, searching for a chemical that would kill clothes moths, carried out trials with dichlorodiphenyl-trichloroethane (DDT) and found that it would kill not only the moths but many other troublesome insects as well. Even more important was the discovery that DDT has a remarkably long-lasting killing effect. The DDT residue on a sprayed surface continues to destroy the insects that come into contact with it for many months after the spraying.

Samples of DDT were procured by both the British and the United States through Intelligence channels and were made available to the Medical Research Council in England, the USPHS, the Armed Forces and others. Investigators with the U. S. Department of Agriculture Laboratory at Orlando, Florida, conducting research with funds provided by the Department of Defense, demonstrated in 1943–44 that anopheline mosquitoes are destroyed for several months when the surfaces on which the insects rest are sprayed once with DDT solutions or water emulsions. These findings were confirmed by investigators in England, by the Allied Armed Forces, the USPHS, the Tennessee Valley Authority and others in various parts of the world.

Eradication of Malaria Becomes Possible

These results definitely indicated the feasibility of utilizing DDT residual spray for the control, and, eventually, the eradication of malaria. With DDT, it is not necessary to hit the insect at the time of spraying but only to spray the surface on which it rests. If, at some time during the essential ten days or longer when the parasites are developing in its body, the insect rests on the DDT residue, it dies before it can transmit malaria. When the malaria-carrying mosquitoes of a community are killed before they have time to become dangerous, transmission cannot occur and malaria fades away. Residual sprays such as DDT accomplish this killing more effectively and cheaply in the average community than any other weapon yet devised. Residual spraying makes eradication practicable.

The advent of DDT made it possible to control malaria economically. Since the residual action of DDT when sprayed on the walls of human habitations was effective in killing anopheline mosquitoes for many months, the expense of malaria control was reduced to the cost of spraying all houses once or twice a year.

When the usefulness of DDT became apparent in 1942–43, the United States and the United Kingdom governments moved at once to make it widely available. So effective were these efforts that over 9.5 million pounds were produced in the United States in 1944 and over 47 million pounds in 1947; in 1959, the U. S. production reached 157 million pounds.

Malaria eradication in the United States. The appearance of DDT coincided with the determination reached in the United States to eradicate malaria. Plans for the use of Paris green larvicide were abandoned; the new insecticide hastened eradication and greatly reduced its cost. In the United States, parts of which were previously highly malarious, malaria is no longer endemic. The only epidemic observed in the past decade was a small outbreak of 35 cases, infected in 1952 by mosquitoes which had fed on a malarious veteran from Korea. During the same period no endemic foci of transmission have been found, in spite of the large number of infected soldiers returning to this country and the relatively large number of infected travelers and

migrant laborers entering the United States annually.

Eradication in Italy. In Italy, well before the end of World War II, Soper *et al.* had experimented with DDT as a house spray, first at Castel Volturno, near Naples, early in 1944, and later the same year at Ostia Lido on the coast. Before the transmission season of 1945, all of the buildings were sprayed in the Tiber Delta and on the Maccarese Plain, where Missiroli had been studying malaria for many years. The cessation of malaria transmission in these areas and the dramatic results obtained with DDT at Fondi after June, 1945, led Missiroli to outline publicly on January 20, 1946, a plan for the eradication of malaria in Italy within five years. Italy's successful nation-wide eradication program began that year (see Annex II) in the Province of Latina, with the very important support of the United Nations Relief and Rehabilitation Administration (UNRRA) in the purchase of DDT and motor vehicles.

In Italy, also, conversations began in 1944 among representatives of the Italian Government, UNRRA and The Rockefeller Foundation relating to a joint effort to eradicate *Anopheles labranchiae* from the Island of Sardinia (Annex II), the most malarious part of the country. Plans crystallized in 1945 and the campaign in Sardinia was inaugurated in 1946. The rapid decline and eventual disappearance of malaria in Sardinia, and in Italy as a whole, once malaria transmission ceased, gave added support to the observation that malaria eradication occurs spontaneously in a very few years when reinfection does not occur.

Eradication in South America. In South America, Gabaldon in Venezuela (Annex II) and Giglioli in British Guiana were the first two malariologists outside of the United States to test spraying houses with DDT, and to realize its potential as an efficient measure for malaria eradication.

Participation of international health agencies. For the international health agencies, anti-malaria activities had a high priority from the first in programs for aid to underdeveloped countries. UNRRA is credited for assisting the first European national programs in Greece and in Italy which led to malaria eradication in Italy and to near success in Greece. The UNRRA program came to an end soon after the end of World War II, and other significant financing for anti-malaria work was not forthcoming for several years. A high priority for malaria control was established at the first World Health Assembly in 1948. The annual budgets of the Pan American and World Health Organizations (WHO) were pitifully small; only as the United Nations Childrens Fund (UNICEF) became interested and as Technical Assistance funds became available through the United Nations could these health organizations undertake active collaboration in malaria control.

2. INTERNATIONAL MALARIA ERADICATION

The introduction of DDT obviated the need for expensive drainage and costly larviciding operations, and made it practicable to control malaria in many agricultural areas, where the isolation of dwellings had made other methods of control impracticable. Thus was the door opened to the development of nation-wide control programs. This, in turn, led repeatedly to the confirmation of the observation that malaria, as a mosquito-borne disease, disappears from an infected population within a few years after transmission ceases, and that malaria reappears in cleared areas only when reintroduced by an infected person.

Pan American Malaria Eradication Program

1950 reconnaissance—XIII PAS Conference. In 1950, a Pan American Sanitary Bureau reconnaissance of the malarious countries of the Americas showed that nearly all of the countries with malaria problems were engaged in serious efforts to control it. Malaria was absent from Uruguay; eradicated in Chile, the coastal zone of British Guiana and the United States; and was greatly reduced in Argentina, Brazil and Venezuela; control programs were well advanced in most of the other countries. So rapidly had programs expanded that approximately 50% of the estimated total homes in the malarious zones of the Americas were being sprayed that year, and it was hoped that the remaining homes would soon be included within the program. To initiate further program extension envisaging the possibility of eradicating the disease from the Western Hemisphere, the XIII Pan American Sanitary Conference (1950) recommended that the Pan American Sanitary Bureau stimulate and coordinate anti-malaria programs and arrange economic assistance to individual countries, with a view of achieving the *continental eradication of malaria.*

Difficulties and danger: DDT-resistant Anoph-

eles. Campaigns were expanded by Governments, trained technicians were provided by PAHO/WHO and equipment and materials were supplied by UNICEF to the Caribbean and Central American area and to four South American countries. Malaria control campaigns were initiated in every malarious country of the hemisphere. The disease toppled from its position as the leading public health problem in the Americas. Hopes were high, and the householders' enthusiasm for the method appeared to insure success of the eradication program.

But success was not to come so easily. Unfortunately, the housefly, which was the householder's visible measure of the value of an insecticide, developed a marked resistance to DDT (a phenomenon already reported from Greece, Italy and elsewhere), and the residual spray program lost much of its initial prestige. The publicity given to the rapid reduction in malaria following the introduction of residual spraying resulted in the general conviction that malaria was no longer an important problem and could be disregarded with safety.

1954 reconnaissance. A second reconnaissance by the Pan American Sanitary Bureau in 1954 showed that large numbers of homes in malarious areas were not included in control programs. Authorities reacted to other fiscal pressures and were reluctant to appropriate funds for controlling a disease which seemed to cause but little damage. This situation, disappointing as it was, might have been accepted for the time being had it not been for the threat inherent in the development of resistance to DDT by certain species of *Anopheles.*

Urgency of eradication recognized. It was most unfortunate that resistance developed before malaria had been eradicated, as the pre-DDT control methods had proven too expensive for general use in rural areas, and were, therefore, limited to urban and village application. It was evident that malaria should be eradicated from the Americas before anopheline resistance to insecticide became insurmountable.

XIV Pan American Sanitary Conference acts on eradication. Government representatives at the XIV Pan American Sanitary Conference in 1954 recognized the danger of prolonged control programs and the consequent hazard of the development of DDT-resistant strains of *Anopheles.* They called upon the Bureau to develop immediately a program of continental eradication to meet the threat. The Conference recognized the need, as the eradication program progressed, to consider measures to prevent the immigration of infected persons into areas already free from infection. The Conference stressed the utmost urgency in achieving the continental eradication of malaria, and urged the member governments to convert immediately all control programs into eradication campaigns.

Conversion from control to eradication. Realizing the seriousness of the situation and the need for quick action, the XIV Conference, 1954, authorized an immediate annual increase of $100,000 to enable the Bureau to implement the Resolution of the XIII Conference of 1950—". . . to provide for greatest intensification and coordination of anti-malaria work in the hemisphere, stimulating existing programs, facilitating interchange of information and furnishing technical and, whenever possible, economic assistance to the various countries with a view to achieving the eradication of malaria from the Western Hemisphere." Considering the obvious inadequacy of this sum for financing active collaboration with governments in the extension of national programs, the Conference called upon the Director of the Bureau to secure the financial participation of organizations, public and private, national and international, in financing its malaria eradication activities.

World Malaria Eradication Program

Executive Board of UNICEF and UNICEF/WHO Health Committee. The mandate of the XIV Pan American Sanitary Conference in October, 1954, was followed in January, 1955, by the decision of the Government of Mexico to undertake the eradication of malaria. Mexico's appeal to UNICEF in March, 1955, for assistance in its eradication program led to the decision of the Executive Board of UNICEF to consult the UNICEF/WHO Joint Committee on Health Policy as to the suitability of malaria eradication for the use of UNICEF funds in the field of health. The Joint Committee met on May 1 and enthusiastically approved the inclusion of malaria eradication among the programs worthy of UNICEF support.

VIII World Health Assembly acts on global eradication. In Mexico City, a few days after the action of the UNICEF/WHO Joint Committee, the VIII World Health Assembly considered the action of the XIV Pan American Sanitary Conference and the recommendations of the WHO

Malaria Conference for the Western Pacific and South-East Asia Regions (November, 1954) and decided that "The World Health Organization should take the initiative, provide the technical advice, and encourage research and coordination of resources in the implementation of a programme having as its ultimate objective the world-wide eradication of malaria."

The Assembly established a Malaria Eradication Special Account to receive and use special voluntary contributions from whatever source for financing WHO malaria eradication efforts.

UNICEF support. The action, in 1955, of the representatives of the nations of the world in the governing bodies of UNICEF and of WHO showed that the peoples of the world greatly desired to be freed of malaria. Most were able and willing to provide for local costs, but found it impossible to purchase insecticides and equipment from abroad with their depreciated currencies. As the global eradication campaign got under way, UNICEF not only accepted the eradication concept but declared that henceforth it would no longer supply insecticide and equipment for malaria control, but only for eradication. This provided a great stimulus to malaria eradication, and UNICEF's continuing sizeable assistance and moral support are heartening encouragement to those who believe that the eradication program must not stop until world-wide coverage has been achieved.

USA support. In 1956, the International Development Advisory Board (IDAB), stimulated by the concerted action of PAHO, UNICEF and WHO, made a study of the possibilities of malaria eradication in the countries in which ICA conducted co-operative malaria control programs. The Board recommended the conversion of all existing control to eradication programs, and that all new anti-malaria work be developed on an eradication rather than a control basis.

In the course of its study, the IDAB undertook to estimate the over-all cost of the eradication of malaria from a selected list of some sixty countries of immediate interest, and concluded (IDAB Report, April 13, 1956) that "a widespread malaria eradication project during the years 1957–61, inclusive, could be carried out for a five-year total of about $519 million," including the expenditure by each national government for its malaria eradication program.

It was obvious that the resources of PAHO, WHO and UNICEF were inadequate to meet the cost of technical orientation and coordination and the importation of insecticides, materials and motor transportation for eradication programs on a global basis. An initial contribution of $1,500,000 was made by the United States to the PAHO Special Malaria Eradication Fund in Fiscal Year 1957; later the Congress approved the ICA plan for U. S. malaria eradication assistance to a number of countries on a bilateral basis, and for an annual contribution to the Special Funds of the PAHO and WHO for a five-year period. In December, 1957, WHO received its first special contribution from the U. S. for the eradication program, and the PAHO a second contribution.

The action of the Congress, in 1957, sponsoring malaria eradication in the Mutual Security Act, was a major step in the development beginning with the war-time creation of the Institute of Inter-American Affairs (IIAA, 1942), previously referred to, followed by the Marshall Plan for Europe (1948) and the Point IV Program (1949), now embodied in the International Cooperation Administration program.

Under the administration of IIAA in the Americas, and elsewhere under the Economic Cooperation Administration (ECA), Mutual Security Agency (MSA), Technical Cooperation Administration (TCA), and Foreign Operations Administration (FOA), malaria control continued to hold high priorities in foreign aid programs, in the late 1940's and early 1950's in both hemispheres and on both sides of the equator. The International Cooperation Administration (ICA), the successor of FOA, with which IIAA is now integrated, continued this emphasis on malaria control, and in due course, has supported the concept of eradication and has transformed control to eradication projects. Over sixty million dollars ($60,000,000) was spent by the United States on malaria control in other countries from 1942 through Fiscal Year 1957, prior to the initiation of malaria eradication.

With the adoption by the United States Government of a policy of supporting malaria eradication, ICA undertook to assist co-operating Governments in converting malaria control projects to eradication. In the three-year period beginning July 1, 1957, the United States, through ICA, expended over $85 million (Table 2) in co-operative malaria eradication projects and in contributions to the Special Malaria Funds of PAHO and WHO. The United States

support provided technical assistance, training, research and provision of commodities (such as insecticides, vehicles, sprayers and laboratory equipment). United States support has been essential to the development of malaria eradication, as it is today. In terms of the long-term welfare of mankind, malaria eradication may be the most significant program sponsored by the United States foreign aid policy.

3. PROGRESS IN MALARIA ERADICATION

The introduction of the residual insecticide, DDT, during World War II provided a new approach to effective malaria control, and paved the way for national, regional, and world-wide malaria eradication. The decision of representatives of governments, meeting in the Pan American Sanitary Conference in 1954, and in the Executive Board of UNICEF and the World Health Assembly in 1955, to unite in the common cause of malaria eradication, has no precedent in the history of mankind. The declaration by the Congress of the United States in 1957 of "the policy of the United States to assist other peoples in their efforts to eradicate malaria" is the first declaration by any nation of war against a disease afflicting the human race. United States support, through both bilateral and multilateral channels, has been of outstanding importance in the signal progress achieved in recent years in the struggle to abolish malaria.

Acceptance of the malaria eradication concept is vital to the success of the global program, which requires that all pockets of endemicity anywhere in the world be wiped out, removing all foci of transmission and sources of reinfection.

Global Acceptance of the Concept of Eradication

Fortunately, this concept has been accepted, in principle, by virtually every country in the world. Some 18 geographical or political units (listed as separate entities by the 1958 UN Demographic Yearbook) have completed the job. Sixty-six other such political units have eradication programs; of these, 20 have large and populous areas where malaria is no longer found and 22 others have previously malarious areas where new infections no longer occur. Thirty-two other countries and territories are preparing malaria eradication campaigns.

USSR and eradication. The USSR has been engaged in eradication since 1952 and has scheduled its completion by 1962. It has called attention to the dangers of reinfection from neighboring countries, and is stimulating the development of eradication programs in Mainland China, North Vietnam and elsewhere.

Summary of National Eradication Projects

Only 37 political units, largely in Africa and Asia, have not yet initiated negotiations for the co-operation of bilateral or international organizations for eradication programs, pilot projects or preliminary surveys. In the Americas, Cuba and Haiti do not have organized eradication efforts. Preliminary steps to eradicate malaria in Cuba and Haiti have now been taken (Table 1).

Of approximately one and a quarter billion people subject to malaria, 280,000,000 live in areas where malaria is reported to have been eradicated, 55,000,000 live where transmission has been interrupted, and 730,000,000 are scheduled to be covered by eradication programs in 1960. Only some 183,000,000 live where no plans of eradication have been formulated (Table 2).

Summary of ICA Bilateral Projects

The progress of malaria eradication in countries assisted directly by ICA is shown in Table 3; of the 24 eradication projects listed, the largest is in India, where it has been estimated that one-third of the malaria problem of the world is concentrated (exclusive of Mainland China). India has over 390,000,000 people living in malarious areas, all of whom are scheduled for protection during 1960. The most advanced ICA program is in Taiwan, where eradication is practically complete. In an intensive survey carried out in 1959, only 167 infected persons were found in an examination of more than 750,000 blood smears; almost all of the positives were old infections.

Administrative and Financial Considerations

Although substantial progress toward the global eradication of malaria has been made, the program has been marked by delays due to technical, administrative and financial problems. While these problems have been expected and are not excessive in view of the magnitude and range of the world-wide program, they must be overcome if eradication is to be accomplished within anticipated time and budgetary limits.

One great difficulty has been the reluctance of governments to establish malaria eradication

TABLE 1

Malarious countries and territories grouped according to their present position regarding eradication—as of January 1960 (data from WHO and other sources)†*

1. *Eradication completed* (18 countries or territories including a population of 108 million living in once-malarious areas)

Barbados	Lithuania (USSR)
Byelo-Russia (USSR)	Moldavia (USSR)
Chile	Martinique
Corsica (French)	Netherlands
Cyprus	Puerto Rico
Gaza Strip	Singapore
Hungary (understood to be eradicated)	Tobago
Italy	Ukraine (USSR)
Latvia (USSR)	United States

2. *Eradication program in operation* (66 countries, 893,501,000 exposed to malaria before initiation of program)

Afghanistan	Guatemala	Philippines
Albania	Honduras	Portugal
Algeria	India	Portuguese India
Argentina	Indonesia	Romania
Bolivia	Iran	Ryuku Islands
Brazil	Iraq	Sarawak
British Guiana	Israel	Spain
British Honduras	Jamaica	St. Lucia
Bulgaria	Jordan	Surinam
Burma	Laos	Swaziland
Cambodia	La Reunion	Thailand
Ceylon	Lebanon	Trinidad
China (Taiwan)	Libya	Turkey
Colombia	Malagasay (Rep. of)	UAR—Egypt
Costa Rica	Mauritius	UAR—Syria
Dominica	Mexico	Union of South Africa
Dominican Republic	Nepal	USSR
Ecuador	Nicaragua	Venezuela
El Salvador	Panama	Vietnam (Rep. of)
French Guiana	Panama Canal Zone	Yugoslavia
Greece	Paraguay	Zanzibar and Pemba
Grenada	Peru	
Guadeloupe		

3. *Preparing for malaria eradication*

A. *Plan of operation—program suspended*
Haiti (3 million exposed to malaria)

B. *Pre-eradication survey* (5 countries, 85 million exposed to malaria)

Bechuanaland	Pakistan	Somaliland (UK)
Korea (Rep. of)	Saudi Arabia	

C. *Pilot project* (14 countries, 59 million exposed to malaria)

Cameroons, State of	Nigeria	Sudan
Dahomey, Republic of	North Borneo	Togo
Ethiopia and Eritrea	Senegal	Uganda
Liberia	Somalia	Voltaic Republic
Netherlands New Guinea	South Rhodesia	

TABLE 1—*Continued*

D. *Negotiations underway for a malaria eradication program* (12 countries, 62 million exposed to malaria)

Angola	Ghana	Mozambique
Belgian Congo	Guinea	Ruanda-Urundi
Central African Rep.	Malaya	Sierra Leone
Cuba	Morocco	Tunisia

4. *No malaria eradication program yet contemplated* (37 countries, 43 million exposed to malaria)

Aden Protectorate	Ivory Coast (Rep. of)	Nyasaland
Australia	Japan	Papua & New Guinea
Bahrein	Kenya	Portuguese Guinea
Bhutan	Macao	Qatar
Brunei	Maldive Islands	Sao Tome & Principe
Cameroons (Br.)	Mauretania (Rep. of)	Solomon Islands
Cape Verde Islands	Muscat and Oman	South West Africa
Chad (Rep. of)	New Hebrides	Spanish Guinea
Comoro	Niger (Rep. of)	Spanish N. Africa
Congo (Rep. of)	North Rhodesia	Sudan (Rep. of)
Gabon (Rep. of)		Tanganyika
Gambia (Rep. of)		Timor
Hong Kong		Trucial Oman
		Yemen

* Political entities are given as listed by the 1959 UN Demographic Yearbook.

† Data are unavailable on malaria status or planning in Mainland China, North Korea, and North Vietnam.

organizations with the necessary authority and financing as outlined in the administrative section of this report. Eradication requires a high degree of competence and the eradication organization must have sufficient legal and administrative authority to operate efficiently. In many cases, eradication has been attempted through existing malaria control organizations, and often the eradication program has had to struggle with inadequate financing and lack of administrative authority. To be effective, eradication efforts must be given full governmental support and freedom of action; anything less leads to unnecessary delay and serious waste of funds.

The technique of eradication differs radically from that of control. In control one may commence operations in an obviously malarious area and expand slowly until areas of low infection are reached or until funds are exhausted.

Eradication cannot follow such a laissez-faire procedure. Those preparing for an eradication campaign must estimate and budget for each year of at least an eight-year program. The first year is one of preparation and is given over to organization of staff, procuring of equipment and materials, training of personnel, making a comprehensive malariometric survey, and geographical reconnaissance.

Administrative phases of eradication. After this first year of preparation come four years of attack (four years of house spraying with residual insecticide to interrupt transmission and to give time for infection to die out in the human host). The four years of attack are followed by three years of surveillance (final or consolidation phase) to confirm fully the absence of malaria, all within the projected eight-year period.

After surveillance, the national health service must assume responsibility for maintenance until malaria is gone from the world, lest reinfection from abroad take place.

Before the program is initiated, a budget must be assured for staff, equipment, materials, and training in each of these eight years, because any interruption of a national program, after it has been launched, may require a repetition of all four years of attack, adding greatly to the cost of eradication.

In very large countries, it is sometimes necessary, for budgetary or personnel reasons, for governments to divide the country into two or more conveniently sized areas, to commence operations in these areas successively, by stages, rather than attempting full, nation-wide coverage in the first year.

TABLE 2

*Summary of status of malaria eradication by regions and populations (thousands) as of December 31, 1959 (data supplied by WHO)**

Region	Total population	Malaria never indigenous or disappeared without specific anti-malarial measures	Population of original malarious areas	Malaria eradicated	With eradication program				Pre-eradication surveys	Pilot projects	No eradication program under way
					Consolidation phase	Attack phase	Preparatory phase	Total			
AFRO†	154,949	13,722	141,227	1,774	1,848	1,351	—	3,199	680	3,025	132,549
AMRO	395,604	252,190	143,414	53,251	2,156	53,657	27,822	83,635	6,528	—	—
SEARO	558,836	45,483	513,353	—	11,654	414,659	86,814	513,127	—	—	226
EURO	671,067	398,181	272,886	213,845	27,077	16,729	7,735	51,541	—	—	7,500
EMRO	198,540	28,886	169,654	1,081	8,521	12,274	1,936	22,731	120,476	928	24,438
WPRO	864,391	142,372*	57,519*	9,507	4,082	6,279	12,732	23,093	6,000	414	18,505
Total	2,843,387	880,834	1,298,053	279,458	55,338	504,949	137,039	697,326	133,684	4,367	183,218
Per cent			100%	21.5%	4.3%	39.0%	10.5%		10.3%	.4%	14.0%

* Information not available for Mainland China, North Korea, and North Vietnam.

† Refers to WHO Regional Offices for Africa, the Americas, Southeast Asia, Europe, the Eastern Mediterranean, and the Western Pacific.

TABLE 3

Status of malaria eradication programs in countries with ICA bilateral projects*

Areas and countries	Year phase initiated			Population (thousands)							Transmission known to occur but no organized program
	Preparation	Attack	Consolidation	Country total	Total malarious areas	Areas where eradication achieved	Eradication program in operation				
							Consolidation phase	Attack phase	Preparatory phase	Total	
Far East											
Cambodia		57S	60S†	4,800	1,000	0	0	1,000	0	0	0
Indonesia	59S	60S	64S	86,900	75,000‡	0	0	2,663	72,337§	75,000	0
Laos	57S	58S	61S	2,000	2,000	0	0	951	1,049	2,000	0
Philippines	52S	54S	59S	23,122	8,000	0	2,824	5,020	0	7,844	156
Taiwan	52	53	58	10,030	6,750	5,232	1,258	260	0	1,518	0
Thailand		54S	58S	21,474	21,474	0	7,600	7,000	6,874	21,474	0
Vietnam		59S	63S	13,400	11,683	0	0		11,683	11,683	0
Total				161,726	125,907	5,232	11,682	16,894	91,943	119,519	156
Near East and South Asia											
Ceylon	57	58	59	9,386	6,131	0	2,535	3,596	0	6,131	0
India		58S	60S	397,540	390,000	0	1,500	388,500	0	390,000	0
Iran	56S	57S	59S	20,500	13,000	0	4,170	6,894	1,931	13,000	0
Jordan		59S	63S	1,527	980‡	0	550‡	430	0	980‡	0
Nepal	59S	60S	65S	8,910	4,171‡	0	0	0	4,171	4,171	0
Total				437,863	414,282	0	8,755	399,420	6,107	414,282	0
Africa											
Ethiopia	57S	58S	62S	20,000	8,000‡	0	0	250	0	250	7,750
Liberia	60S	61S	65S	1,250	1,250	0	0	350	0	350	900
Libya	58	59	63	1,250	30	0	0	30	0	30	0
Total				22,500	9,280	0	0	630	0	630	8,650

Americas											
Bolivia	56	58	63	3,350	888	0	0	888	0	888	0
Brazil	58S	60S	64	64,007	33,035	3,171	0	4,923	24,941§	29,864	0
Colombia	58	59S	63S	13,823	9,787	0	0	9,787	0	9,787	0
Ecuador	57	58S	62S	4,007	2,346	0	0	2,346	0	2,346	0
Guatemala	57	58S	62S	3,618	1,544	0	0	1,544	0	1,544	0
Haiti‖	57	60	64	3,888	2,800	0	0	0	2,800¶	2,800	0
Honduras	56	59	64	1,888	1,347	0	0	1,347	0	1,347	0
Jamaica	57	58	62	1,689	1,348	0	185	1,163	0	1,348	0
Nicaragua	57	59S	63S	1,461	1,307	0	0	1,307	0	1,307	0
Paraguay	56	59	63	1,672	805	0	0	805	0	805	0
Total				99,403	55,207	3,171	185	24,110	27,741	52,036	0
Grand total				721,492	604,676	8,403	20,622	441,054	125,791	586,467	8,806

* Data taken principally from WHO A13/P&B/15, April, 1960 (draft copy).

† S, malaria eradication being developed in progressive stages. Date represents beginning date for this phase.

‡ Provisional estimate.

§ Includes populations in States where, under staged program, operations have not yet begun.

‖ Attack phase interrupted 1958, planned to resume in 1960.

¶ Plans prepared and approved, but operations not yet begun.

Lessons from Experience

After the experience of the past four years, malariologists are much better able to cope with the technical and administrative problems of eradication in many parts of the world. Especially valuable have been the lessons learned in those countries which have had extensive malaria control programs that were converted to eradication. In some, malaria transmission had been completely interrupted for some years in heavily populated areas; but, when house spraying was discontinued, the disease was reintroduced from peripheral areas which had not been adequately covered. In others, failure to spray all summertime habitations of agricultural workers, to recognize early evidence of extra-domiciliary transmission, to extend the program to all malarious areas as rapidly as resources permitted, and to provide sound administration has greatly delayed eradication and has increased considerably the ultimate cost.

The value of thorough education of the top authorities of governments and the people concerning the methods and objectives of the malaria eradication campaign, of adapting the spraying program to the specific needs of different areas, and of early identification of the problem areas of transmission through adequate epidemiological evaluation is well demonstrated in significant savings of time and money.

The basic lesson learned from these programs is that one cannot plan a complete national program from the beginning and blindly follow the calendar of proposed operations; rather is it important that constant studies be made to identify those areas where transmission ceases immediately after spraying and those where transmission continues. The adaptation of methods to local problems will result in greater efficiency, reduce the period of the eradication program and permit considerable economies.

The development of the technical advisory staff of ICA, PAHO and WHO and their intimate co-operation are making possible the rapid dissemination of the lessons learned in each country.

Importance to Children

UNICEF, which embarked on support for malaria eradication programs in Latin America as early as 1955, recognizes more and more the importance of malaria eradication to the children of the world and is devoting more than a third of its budget to this single program.

Future Prospects

In recent years, the results of field investigations and pilot projects in Africa have indicated that eradication in this continent may not be much more difficult technically than elsewhere (see Tropical Africa).

Outstanding progress in eradication has been reported from all parts of the world. Even more important, the development of technical and administrative ability is producing an atmosphere of optimism and determination in the malarious countries of the world to get on with the job of global malaria eradication. No other proposal for international co-operation in health appears to have had the universality of response that has been accorded to the malaria eradication program.

4. TECHNICAL CONSIDERATIONS

There are relatively few countries in which malaria is transmitted in all the inhabited parts of the country. Breeding places for malaria vectors are not distributed equally throughout a country. Often unfavorably low temperatures are found as one goes into more temperate zones or increasing elevations.

Spraying non-malarious areas is an unnecessary waste of funds, while failure to spray all malarious areas may endanger the success of the entire program. The basic reason for deciding that an area requires spraying is that malaria is locally contracted. The presence of a known vector is of concern only in those areas where malaria transmission occurs. Because of the difficulty, at times, of demonstrating transmission, there has been a tendency to include all areas in which vectors could be found in any number or stage of development. There are few vectors, however, which cannot be found outside the malarious area. Therefore, unnecessary spraying where transmission does not occur wastes time, personnel and materials, adding needless costs to the entire program.

Epidemiological Considerations

Localities with some years of effective malaria control may require shorter periods of complete coverage than do unsprayed areas. Or it may be found that a full-time schedule of eradication spraying must be added to the years of partially effective control spraying. Such decisions must be made in the light of wide experience in ma-

lariology and carefully planned studies, if effective and economical eradication is to be accomplished. A malariologist experienced in one country, must realize that conditions and the resultant malaria problem may be quite different in another.

Global eradication of malaria is planned on the basis of interrupting transmission of the malaria parasite from person to person, rather than through a general attack aimed at eradicating the vector mosquitoes. The objective is reached when transmission has been interrupted with the absence of new infections for such a period of time as is necessary for the old infections to die out spontaneously.

When converting a control program to eradication, two important steps are necessary:

(1) Locate unsprayed, malarious areas. Usally there are fringe areas or isolated places not previously included because they were only moderately malarious or had small populations difficult of access. With an antimalaria organization already in existence, it should not be difficult to determine the additional areas to be included.

(2) Assess the results of any control program to be converted to an eradication campaign. Where malariometric studies show that transmission has not been interrupted, a full program of eradication must be developed as though no spraying had been done in the past. Where the records and malariometric studies indicate the absence of malaria, or its presence only in scattered foci at very low endemic levels, spraying may be judiciously reduced or discontinued. There may be danger in halting spray operations in less than three years after transmission appears to have been interrupted.

Delimiting the malarious areas where careful studies have not been made is difficult. Where delimitation has been hurried to permit cost estimates for eradication planning, great embarrassment may ensue, should the tentative estimates become binding and prove to be inadequate.

Where the entire country is notoriously malarious, preparation of cost estimates are relatively easy. In others, the boundaries of endemic areas can only be indicated approximately by easily recognized geographical or political landmarks.

A study of the available records, discussions with informed national workers and well-pointed field trips should quickly orient one as to malarious conditions in a country. Field observations are adequate to confirm the existence of malaria in moderately and heavily infected areas. A careful study of potential breeding areas, climatic factors and vector habits readily establishes and explains the pattern for the production of malaria. The influence of irrigation, rice culture, fish ponds, salinity of water and other local conditions becomes obvious. With this pattern delineated, one is better able to analyze the malaria situation in the remaining territory.

Delineation of malarious areas to be sprayed. Special attention must be given to the problem of how far spraying should be extended from obviously malarious to nonmalarious areas. When one proceeds to higher altitudes, careful delineation is especially important because difficulty of transportation and relative inaccessibility of population greatly increase the per capita cost of spraying. Where the evidence of malaria is doubtful, and the per capita cost of spraying would be excessive, it may be justifiable to limit spraying operations somewhat in such areas the first year, and let the continued presence of malaria outline the area to be sprayed. If this technique is to be used, very careful entomological and epidemiological observations should be made in the fringe area. Experience shows that in certain areas the small amount of malaria present had its roots in a more malarious neighboring area and disappeared readily during the first year of the eradication program in the source area.

It is obvious that where evidence of transmission of malaria is found during the first year, provision must be made for spraying thereafter.

Determination of the degree of endemicity requires careful sampling procedures with examination of a considerable portion of the entire population. The simple determination as to whether malaria is or is not present, on the other hand, can often be established by much simpler procedures, and even by analogy with conditions known to exist elsewhere. In the absence of information as to the degree of endemicity, all endemicity should call for spraying.

Duration of spraying. The length of time that spraying continues will be determined by epidemiological evaluation during the course of the campaign. In those countries where the degree of endemicity in different areas can be readily established, it may be possible to vary the eradication campaign adapting it to each individual area.

This should result in considerable savings in personnel and funds required for the program as a whole; in areas with minimal malaria, as in the coastal plain of Taiwan, the duration of spraying operations may be shortened. In some areas, two years of spraying may be sufficient, and in others possibly one will be adequate. Any decision for the reduction of the period of spraying should be justified by at least one year of good surveillance without evidence of continuing transmission.

On the other hand, in areas of high endemicity where transmission has been intense, meticulous care should be taken to insure efficient, complete spraying, for the standard four-year period, of all dwellings and sleeping quarters within the malarious area.

In determining malarious areas, the possibility of periodic epidemics invading areas where in normal years malaria is practically non-existent must be kept in mind; where such areas are not to be sprayed, careful observation should be maintained until malaria has been eradicated from neighboring areas from which these epidemic areas might be reinfected.

Fringe and mobile populations. Experience in eradication programs has demonstrated conclusively the necessity of carrying measures of prevention to all elements of the exposed population, rather than the all too common practice of reaching only the easily accessible populations. One of the great advantages of the eradication concept is the mandatory obligation to carry the benefits of preventive medicine to fringe populations living in isolated and sparsely settled areas, often hilly and of difficult access both to the sprayman and to the supervisor. Failure to include these fringe populations in malaria eradication programs has delayed eradication in a number of countries. A common observation has been the rapid decrease of malaria during the first two years of the eradication program in the readily accessible and heavily populated parts of a country, with some reduction of malaria in the fringe areas but with transmission still continuing there. Where this occurs, eventual interruption of spraying leads to reinfection of the clean areas and forces the reorganization of spraying operations in the "discontinued" areas.

Even the best administered service, with one hundred per cent efficiency in blocking transmission, will fall short of eradication if coverage is limited to the area occupied by 95% of the exposed population. On the other hand, a less efficient service throughout the entire malarious area of the country may succeed, if operating with sufficient frequency over an adequate period of time.

Indigenous tribes living in isolated regions, some of whom have never figured in the national census, constitute important problems for malaria eradication programs. Each situation requires special study, and eventually, the collaboration of the leaders of the tribe for its solution. The possibility of eradicating malaria through drugs administered in table salt supplied to an entire area is being tested in different parts of the world. General formulae cannot be written for the special problems met in different regions; each special problem must be studied carefully to determine the proper measures to be applied.

Similarly, the movements of lumbering and road construction gangs, and of migrant and seasonal laborers, can best be followed by inspectors resident in and responsible for a definitely delimited geographical area. Migration is understood in this context to refer to the movement of populations seasonally from one part of the country to another or even from one country to another across an international boundary line, when such movement is associated with the seasonal harvesting of crops, grazing or other agricultural activities. Immigration for our purposes refers to the more limited passage from one country to another of individuals who are not part of a regular rhythmical movement of population.

The term labor movement, has been introduced to refer particularly to the movement of large numbers of young men for limited periods as from one part of Africa to another, in connection especially with mining or industrial operations. Technically, the problem posed by the reinfection of "eradicated" areas by the movement of population is the same whether such movement of population be within the borders of a given country or across frontiers. In each case, the population exposed to reinfection must promote the eradication of malaria in the areas from which the reinfection threatens, whether the threat comes from within or from outside the country. Once eradication starts in a given country, that country automatically acquires a stake in the eradication of malaria in all countries and especially in those from which it may be reinfected readily. In the same way, within the country itself, eradication does not permit the neglect of any segment of population exposed to infection.

The reinfection of "eradicated" areas by migrant workers, then, is best handled by the extension of eradication measures to cover the point of origin of the moving population. The United States, where a number of cases of malaria have regularly occurred in the past in connection with encampments of migrant laborers from Mexico, is benefiting from the Mexican eradication program through a reduction, and presumably in the near future, the disappearance of this source of reinfection.

Until the last decade and a half, malaria was essentially a problem for the local community where it existed, and by no stretch of the imagination was it ever considered solvable by isolation or quarantine measures. With the development of eradication techniques, however, communities which continue to have malaria constitute a threat of reinfection to "eradicated" areas.

a. *Immigration.* With evidence of the importance of the reintroduction of malaria parasites into communities which have been freed, there has developed a demand on the part of certain governments for the adoption of international measures which will enable malaria-free areas to protect themselves against reinfection from malarious areas (*e.g.*, the action of French Guiana at the XIV Pan American Sanitary Conference, 1954). The first international meeting for the discussion of this point was called by the World Health Organization in Athens in 1956, and future meetings are anticipated.

b. *Pilgrimages.* The annual pilgrimages to Mecca from all parts of the Moslem world have been notorious for their influence on the spread of smallpox, cholera, and other infectious diseases. The threat of pilgrims carrying malaria from one country to another will decline as malaria eradication programs proceed in certain countries and as the tendency to use airplane transportation increases. But, in the meantime, the pilgrims who set out for Mecca, particularly overland, must be considered as possible sources of reinfection to "eradicated" areas, en route.

c. *Nomadism.* Malaria exists in many countries where nomadism is the way of life of many thousands of people. Nomadism presents a definite obstacle to the easy eradication of malaria by the routine application of residual insecticide to human habitations. The facts that people are without fixed habitations, use such portable dwellings as tents, and move about during certain months of the year completely out of touch with population centers, increase the difficulties.

Among the measures to be stressed are (1) complete interruption of transmission in villages near which the nomads camp; (2) regular spraying of tents and temporary huts and shelters; (3) mass drug therapy, perhaps by medicated salt, when the tribes sojourn in their fixed sites; and (4) selecting and training spraymen and surveillance agents from among the tribesmen, to work among them especially during the migration period.

In certain areas, the study of the habits of the nomads and the movements from place to place may reveal situations which can best be handled by larviciding, that is, by an attack on the limited breeding places of the vector in arid and semi-arid regions, rather than by attempting to spray the habitations of the nomads or to attempt the eradication of the parasite by drug treatment. In areas where mosquito breeding is limited in space and occurs only during certain weeks or months of the year, it may prove relatively simple to eradicate vector species from desert areas rather than to maintain permanent control. A restudy of the data on the rapidity of *Anopheles gambiae* eradication from Brazil, once a satisfactory technique had been established, and on the speed with which *Anopheles gambiae* disappeared from the Nile Valley in Egypt between November, 1944, and March, 1945, (the last *Anopheles gambiae* found in Egypt was collected on February 19, 1945) may lead to a reconsideration of the use of larvicides rather than residual insecticides in many areas where nomadism is a problem.

d. *Fringe habitations.* Special administrative effort is needed to establish definite individual responsibility of employees of the Malaria Service for searching out and spraying in definitely delimited geographical areas all fringe habitations and temporary shelters as (1) the huts used by farmers during periods when they are gardening or harvesting their crops at a distance from their homes, for example, the "rice kitchens" in Liberia and the "farm kitchens" on Zanzibar; (2) the huts of farmers who try to remain inconspicuous in relatively inaccessible places because they are raising narcotics, illegally clearing land, or otherwise contravening the law; (3) the dwellings of pioneers who push out into previously underdeveloped areas, often because their former home communities in contiguous areas become crowded following interruption of malaria transmission;

and (4) shelters in which hunters, woodcutters, fishermen, road workers, forest guards, vacationists, etc., sleep from time to time.

In some countries, planes or helicopters may be borrowed or hired for use in scouting out isolated habitations. In all malaria eradication programs it is important to have adequate provision for finding all fringe habitations in which persons may become infected with malaria.

Special attention must be given to fringe areas to insure their adequate coverage by the Epidemiological Evaluation Service. These areas merit continuing surveys to determine when malaria transmission ceases.

Entomological Considerations

The successful eradication of malaria by the spraying of residual insecticides is based on the habits of the important anopheline vectors, which in most areas of the world, characteristically invade human habitations in search of blood meals. After feeding, the engorged mosquitoes rest upon walls and ceilings of dwellings where they absorb lethal doses of DDT or other residual insecticides. Careful study of a few vector species, indicates that from one to fifteen minutes of actual contact with a DDT deposit is required to produce 100% mortality in normally susceptible insects. The residual spraying procedure is so effective that vectors which both feed and rest indoors, such as *Anopheles sacharovi* in Israel and *A. darlingi* in coastal British Guiana and in Venezuela, have been virtually exterminated by properly conducted campaigns.

Outdoor feeding and resting habits of vectors. There is a wide variety of feeding and resting habits of the various vector anophelines. A good example is *A. gambiae*, the most important vector in Africa. During its excursion to Brazil in the 1930's, this species was found to feed only at night and always indoors, as in much of its range in Africa; after feeding, it rested indoors. In Uganda, however, it is known to attack man outdoors even at mid-day as well as at night, and blood-fed, engorged females are frequently found in outdoor resting places.

This type of natural behavioristic avoidance of houses is believed to have prevented the complete interruption of malaria transmission by residual spraying in Trinidad in the case of *A. bellator*, an important vector which readily feeds on man in shaded woods during the day and invades human bedrooms only infrequently; and also with *A. aquasalis*, *A. cruzi-cruzi*, and *A. nuñez-tovari* in South America. *A. sundaicus* in part of Indonesia has been reported as avoiding DDT- and dieldrin-sprayed walls; *A. sergenti* in Jordan has also been observed to feed and rest outdoors. Residual spray operations will not be effective in such areas.

As more and more areas of the world are drawn into the global residual spraying campaign against malaria, other examples of such natural behavioristic avoidance among anopheline vectors of malaria may be found. Additionally, there is evidence of the *acquired* trait of behavioristic resistance by such vectors as *A. albimanus*, *A. darlingi* and *A. sacharovi*. Strains with such behavioristic resistance have an apparent hyperirritability to DDT residues and therefore do not rest on treated surfaces long enough to acquire lethal doses of the insecticide.

It is apparent that where the dominant malaria vector in an area is one which exhibits either natural behavioristic avoidance or acquired behavioristic resistance, the normal methods of residual spraying will not be fully effective. This emphasizes the need for adequate entomological and epidemiological studies during all malaria spraying programs. On the basis of the information obtained it may be necessary to introduce supplementary eradication measures such as the use of persistent fumigants, larviciding, or chemotherapy.

Insecticide dosage and cycle. The principla method of achieving malaria eradication is the application of residual insecticides to habitations and animal shelters nearby to destroy the vector mosquitoes and thus prevent transmission of the malaria parasite. DDT, dieldrin, and, to a much lesser extent, BHC are the residual insecticides used to date in malaria eradication. For logical reasons, there have been wide variations in the dosages and spraying cycles used for malaria control in different countries. On the other hand, there has been a tendency in some cases to adopt dosages and spraying cycles based on a precedent set in early control and eradication programs. Further research and experience have shown that in many instances a dosage of one gram of DDT per square meter (1 g/m^2) instead of the two grams per square meter (2 g/m^2) used in the early programs, is adequate.

a. *Effect of transmission period.* The periodf o transmission of malaria in a given area may profoundly affect the spraying schedule. If this

period is found to be no longer than six months, every effort should be made to concentrate the spraying in the two months before the season begins, so that one spraying a year would be adequate. Where transmission may occur at any or all seasons of the year, as in many tropical areas, planning should be for at least two sprayings a year, whether concentrated in short periods because of the local labor supply or continuously throughout the year with a constant force of spraymen. Varying physical factors—climate, materials used in the walls that are to be sprayed, and others—affect the residual effectiveness of the insecticide, prolonging it in some areas and shortening it in others. Cost calculations are based on averages and what is lost in one area may be gained in another.

b. *Other factors.* In determining the dosage and, to some extent, the number of sprayings each year, consideration must be given to other factors that affect malaria transmission. Some of these are: (1) efficacy of insecticidal residue against the specific vectors involved; (2) thoroughness of treatment; (3) completeness in spraying all houses in the eradication area; (4) habits of vector in relation to host and treated surfaces; (5) modification of, or additions to, houses after spraying which reduces effectiveness of residual deposit; (6) influence of surface on residual action of deposit; (7) circumstances which influence efficacy of deposits (humidity, soot, painting, papering, etc.); (8) climatic conditions of country; (9) seasonal abundance of vector; and (10) incidence and availability of infected human hosts.

c. *Insecticide dosage.* Accurate and adequate information on the foregoing elements was not available for all countries and all vectors before malaria control and eradication operations were begun. In some countries, DDT dosages have ranged from 0.25 to 2.6 g/m² and application intervals have varied from 6 weeks to 12 months. With dieldrin, the dosages have ranged from 0.25 to 1.2 g/m² and the number of applications per year from 1 to 2. Despite the reportedly successful use of these wide ranges of dosages and spraying cycles, most countries have used DDT at 2 g/m² applied every 6 months and dieldrin at 0.6 g/m² at yearly intervals.

To aid countries in their selection of dosages and spraying cycles, the WHO Expert Committee on Malaria and the WHO Expert Committee on Insecticides have supplied information from time to time on field use experience and on laboratory tests with these insecticides. Unfortunately, those directing the malaria programs in some countries gained the impression that the WHO committees recommended for universal use standard dosages of DDT at 2 g/m² applied every 6 months and dieldrin at 0.6 g/m² every 12 months, and there has been a tendency to hold to these dosages and spraying cycles without regard to the ten factors mentioned above.

The Panel has noted that India is making excellent progress in malaria eradication with DDT at a dosage of 1 g/m² every 6 months. Laboratory data have indicated little difference in 1 or 2 g/m² of DDT for 6 months after application. Likewise, field and laboratory data indicate 0.25 g/m² of dieldrin to be satisfactory for 6 months at least against some malaria vectors in some countries. Experience in many areas has shown that the erection of new homes and frequent changes in wall surfaces after spraying make it desirable to repeat spray coverages at least as often as every 6 months. On the basis of these considerations, the Panel recommends that the standard treatment for malaria eradication be one gram of DDT per square meter applied every 6 months. The Panel fully recognizes that this standard dosage and spraying cycle will not be suitable for all situations throughout the world, but it believes that they should be used until entomological and epidemiological studies show that other dosages, other insecticides, and other schedules of application are indicated.

d. *When resistance appears.* In the case of resistance to DDT, the Panel recommends that dieldrin be used at the rate of 0.25 g/m² every six months unless adequate data are available to justify a different dosage and spraying cycle. The appearance of resistance to DDT in localized areas should not be the signal for a country-wide change to dieldrin. The latter should be used only in the specific areas where resistance to DDT has been demonstrated.

In the case of dual resistance to both DDT and dieldrin, malathion is presently recommended as a substitute. Malathion should be used only in those specific areas where resistance to both DDT and dieldrin have been demonstrated and should be applied at 1 g/m². On wood and paper surfaces, this dosage is effective for six months, but on mud, thatch and certain other types of surfaces, applications should be repeated every three months. Since these recommendations are based on limited field tests, entomological and

epidemiological studies should be made to determine if these suggested dosages and spraying cycles are adequate in the specific areas where malathion is used.

e. *Need for epidemiological studies.* Because of the complexities of the factors which determine the duration of effectiveness of a residual spray application in any given area, adequate epidemiological and entomological studies should be conducted in each country, along with spraying operations, to obtain the necessary information essential for the effective and efficient use of the insecticides. In those countries where malaria eradication has not yet begun, it is desirable that such studies be included as part of the planning phase of the program. These should be considered as an integral part of the over-all program and should be provided for in the budgeting for malaria eradication.

Resistance to Insecticide

Definition. "Resistance to insecticide" is the term applied to a phenomenon whereby an insect species or population becomes able to survive exposure to dosages of insecticide previously fatal to it. Physiological resistance is due to the ability of some or all insects of a population to withstand the action of the insecticide. In the case of susceptible populations, selective killing of a large number of susceptibles permits increased opportunities for the very small number of resistant individuals to interbreed and later predominate.

Behavioristic resistance is due to a change in behavior whereby the insects avoid lethal contact with the insecticide. When the proportion of the resistant strain becomes sufficiently large, the insecticide fails to achieve the desired reduction in insect numbers.

Specificity. Resistance in insect strains is generally specific to the insecticide to which the insect population has been exposed for a number of generations. However, resistance may develop concurrently without prior exposure to closely related chemical analogues. For example, houseflies highly resistant to DDT are also generally resistant to the DDT analogues, methoxcychlor and TDE. Such resistant strains may remain susceptible to less closely related chlorinated hydrocarbons, such as lindane or dieldrin. Subsequent exposure, for a period of several generations, to such insecticides may lead to strains resistant to both types of chlorinated hydrocarbons. Presently, most DDT-resistant vector species are still susceptible to dieldrin, although there are some instances where resistance has developed to both insecticides. In those instances DDT-dieldrin resistant species are susceptible to organophosphorus insecticides.

Agriculture. An important facet of the resistance problem is the fact that DDT, dieldrin, and BHC—the materials used in house spraying for malaria control and eradication—are also used widely in agriculture. The dusting of crops contaminates nearby waters, breeding places of anopheline mosquitoes, thus exposing the larval stage also to the insecticides. In such areas the malaria vectors may be exposed both as adults and larvae, and this is known to have accelerated the development of resistance in some species. For example, *Anopheles quadrimaculatus*, the principal malaria vector in the United States, developed resistance to dieldrin, BHC and related compounds in Mississippi solely as the result of their use in agriculture. As agriculture expands in the less well developed countries, agricultural use of insecticides can be expected to be of increasing importance as a factor contributing to the development of resistance.

Discovery of resistance. Insecticide resistance in an anopheline vector of malaria was first suspected in *Anopheles sacharovi* in Greece in 1949 but was not confirmed for several years because of the lack of an adequate quantitative evaluation technique. Quantitative evaluation techniques are now available for prompt detection of resistance in mosquito larvae and adults.

Urgency. The appearance of resistance in anopheline vectors of malaria was one of the compelling factors in the decisions of the Pan American and World Health Organizations, and of ICA, to sponsor malaria eradication, hoping to achieve it before the potential danger of resistance in malaria vector species materialized. At that time, physiological resistance had been reported in seven vector species.

The policy makers and planners of these organizations did not overemphasize the potential danger of the resistance problem becoming more severe and widespread. This is evidenced by the fact that by the end of 1959, resistance had been detected in 21 anopheline species in 29 different countries (Figure 1). Of these, one species is resistant to DDT alone, 13 to dieldrin alone, and 7 to both DDT and dieldrin. In most cases this resistance is still in the incipient stage and is

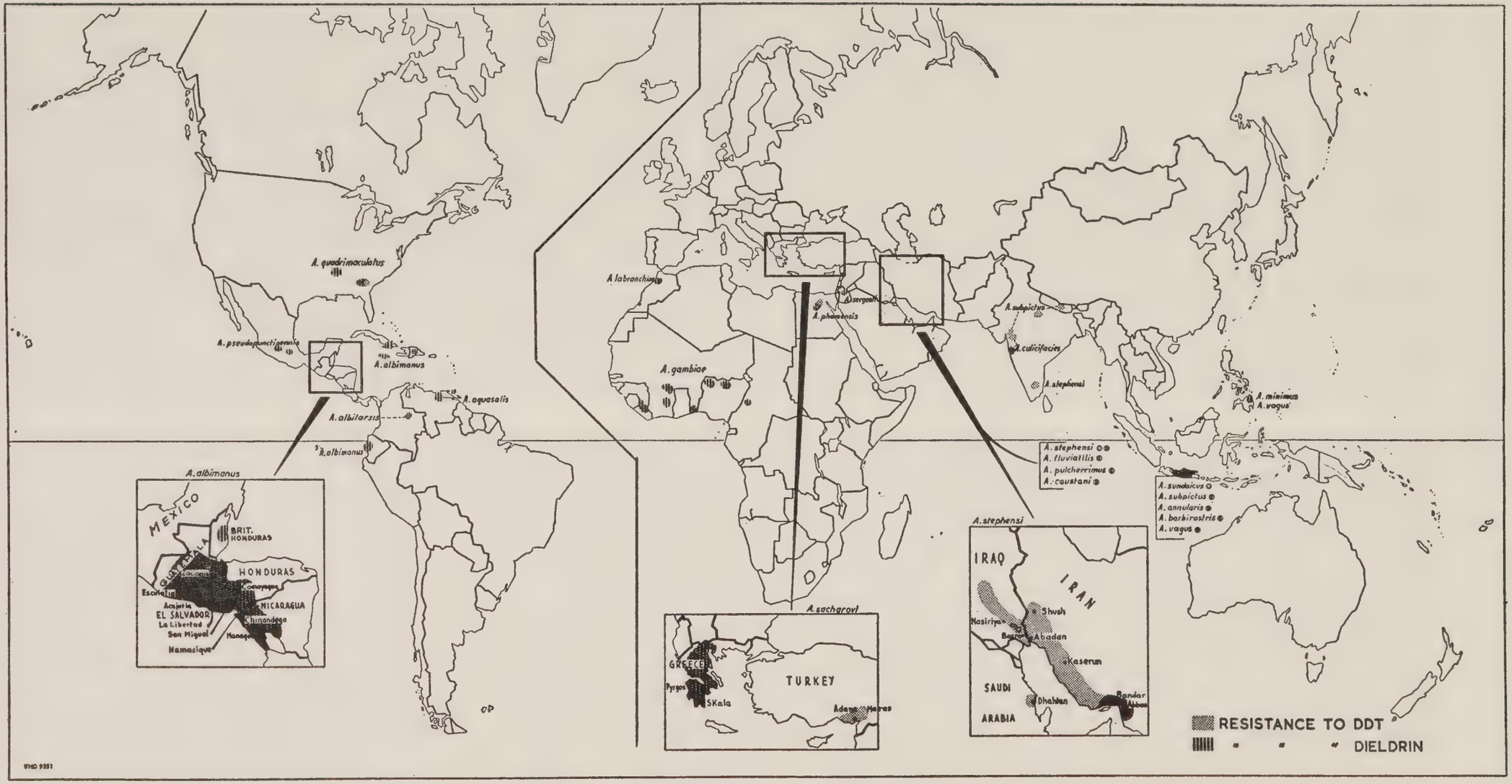

FIG. 1. Insecticide resistance in anopheline mosquitoes

limited geographically to relatively small portions of the range of affected species of *Anopheles*. It can be expected to spread geographically if there is continued use of the insecticide.

Effect on program. The Malariologist faces a dilemma in any area where resistance to DDT appears for the first time. Previously, it would have been recommended that dieldrin be substituted immediately for DDT. However, experience has shown that resistance to DDT may spread very slowly (*e.g.*, in Indonesia), whereas resistance to dieldrin may develop very rapidly. It has also been found that dieldrin is much more toxic to employees of the eradication service. Consequently, it is the opinion of this Panel that localized resistance to DDT should not be the signal for a country-wide shift to dieldrin. Rather, the change should be made only in areas where DDT resistance is clearly recognized. Elsewhere DDT should be continued until resistance has been determined by field evaluation. Such field evaluation should be a continuous integral part of the eradication program.

This Panel recommends that DDT be the insecticide of choice until significant resistance to it is demonstrated. Dieldrin should be the first choice as a substitute for DDT, but should be used only in the specific areas where resistance to DDT is known to occur. Where resistance to both DDT and dieldrin occurs, it will be necessary to use malathion, currently the most acceptable of the organophosphorus insecticides. The Bayer Compound 29493 (Baytex) is also effective against mosquitoes, but is more expensive, is several times more toxic to man and animals and has not been so widely applied, with complete safety, as has malathion.

The impact of resistance on malaria eradication programs is due to several factors. DDT is a cheap, safe, long-lasting insecticide. Any known substitute for it involves one or more objectionable features such as increased toxic hazards to man and domestic animals, increased cost and shorter residual effect. Dieldrin can be used at approximately the same cost since lower dosages are used and under some conditions is about equal to DDT in lasting qualities. But even when used at lower dosages it is more toxic to man and has produced numerous cases of poisoning among spray operators where adequate precautions have not been observed. None of the organophosphorus compounds currently available for possible use in malaria eradication are as long lasting as DDT or dieldrin, and they are more expensive to use, owing to the higher prices of the insecticide and the increased labor and equipment costs of more frequent applications. Based on current prices of available substitutes for DDT or dieldrin, it is estimated that the over-all cost of house spraying will be increased at least fourfold in those areas where resistance forces a change to malathion. Even with a satisfactory substitute immediately available when resistance develops, the logistics involved in changing insecticide cause some slowing of the eradication program, thereby extending the time required for eradication.

Cost effect. Resistance has already been a factor in increasing costs for certain ICA bilateral programs. It has been recognized in parts of slightly more than half the countries participating in the bilateral malaria eradication programs. The problem is particularly acute in Central America, where resistance to both DDT and dieldrin poses an immediate operational problem. It is important in other countries and can be expected to become more significant in the future.

Need for research. ICA is actively supporting research at the Public Health Service Laboratory at Savannah, Georgia, and WHO has recently inaugurated an international collaborative research program involving seven laboratories in the United States, Great Britain and Africa, to develop other suitable substitute residual insecticides, and other eradication techniques.

While resistance is not now an insurmountable obstacle to malaria eradication, the Panel believes that every effort should be made to initiate effective malaria eradication programs in all areas as soon as practicable in order to make the most rapid progress while there is still minimal resistance to DDT. The Panel further believes that it is essential for ICA to continue its support of research to develop new insecticides and that adequate funds and personnel be provided on all bilateral programs for field observations on the habits of malaria vectors, and variations in their susceptibility to the insecticides used.

Chemotherapy

Malaria eradication programs have thus far depended almost entirely on the domiciliary application of residual insecticides. Where these can be used cheaply and where vector mosquitoes bite man indoors and rest on sprayed walls within houses, the procedure is effective. There are malarious areas, however, where the vector has

acquired resistance to insecticides, where residual spraying is ineffective because people live in houses without walls, where the vector bites and rests out-of-doors, where the mores of the people prevent the effective use of residual sprays and where logistic problems make the procedure too expensive. Under certain conditions, mass chemotherapy may be the most effective way of stopping transmission. Moreover, it may be desirable to use drugs to eliminate foci of infection during the surveillance phase of the program when mass therapy may be limited to infected individuals and small groups of isolated contacts.

Mass chemotherapy. Mass chemotherapy calls for the administration of a drug, or drug combination, at regular intervals, over a considerable period of time, to every member of the population at risk. This can be done by giving the medicine in a pill or tablet or by combining it with a universal article of diet, such as salt. The first method is traditional; people are accustomed to taking medicine in tablet form and are generally willing to do so under supervision. The other method is relatively new, but as acceptable as the salt that hides it. It was first proposed by Pinotti in 1952, and under favorable conditions has proved highly effective.

Effect of life-cycle. In moving into the field of chemotherapy, eradicationists must take cognizance of differences in susceptibility to various drugs in each of the four life-cycle forms of the three species of malaria parasite, *Plasmodium vivax*, *P. falciparum*, and *P. malariae*. The four forms in the life-cycle of the parasite in man are: the asexual erythrocytic form, the sexual erythrocytic form (gametocyte), the sporozoite, and the exoerythrocytic form. The form most frequently seen is the asexual erythrocytic form which inhabits the red blood cell. During this cycle some plasmodia differentiate into sexual forms (gametocytes), male and female, which mate in the stomach of the mosquito and form oocysts. When mature (about ten days) they release sporozoites (or sporonts), which reach the insect's salivary glands and are ready to infect a human being when injected with the bite. Within a few hours after injection these sporonts are filtered out of the blood stream and are deposited in the liver, where they develop into exoerythrocytic schizonts.

Upon maturing, these schizonts release merozoites which are introduced into the blood stream to take up abode within red blood cells (erythrocytes), where they become full grown in about 48 hours, bursting, releasing daughters, each to seek a new erythrocyte—and at the same time pouring out the accumulated toxins to which the human body normally reacts with a severe chill and high fever. Thereafter the cycle repeats itself.

Individuals or small groups receive drugs for only a short time when chemotherapy is used during the period of surveillance. Whether given to large populations, small groups, or individuals, the object is the same, namely, to stop transmission through *sporontocidal*, *suppressive*, and *curative* effects on existing infections. Because of the selective action of available drugs, it is generally impossible to obtain all three of these ends with a single compound.

Sporontocidal effect. The 4-aminoquinolines (chloroquine, amodiaquin, *et al.*) have no effect on the infectivity of mature gametocytes. The sexual forms of *P. vivax* and *P. malariae* are removed from the circulating blood along with the asexual forms and no new ones develop as long as an effective drug blood level is maintained. However, mature *P. falciparum* gametocytes may remain in the blood stream and be infective to mosquitoes for several weeks.

Pyrimethamine and proguanil produce a decided sporontocidal effect on gametocytes of all species within a few hours, and primaquine has a similar effect which is almost as rapid. The first two drugs may provoke resistance in the parasite, a characteristic not shared by primaquine. But the latter is quickly eliminated and therefore its action is of short duration.

Suppressive effect. Quinine, the only effective antimalarial for almost 300 years, has been superseded by more effective, less expensive, less toxic, and longer acting synthetic compounds. Quinine is not recommended except in areas where the economy of the country virtually demands its use. Quinine stops acute attacks, but does not cure the infection, which continues to relapse, and so can play no part in eradication. Quinacrine, the first of the effective synthetic compounds, has been superseded because of toxicity and the necessity for frequent administration. Proguanil has been highly effective in some areas, but the appearance of resistance has limited its usefulness. Pyrimethamine, the most effective of all antimalarials in terms of dosage, has produced outstanding results in many areas of the world. This drug was employed once-

weekly in Venezuela over a very large area embracing over one hundred thousand people. Outstanding results were evident after the first month; no evidence of transmission was found after the third month; and this situation continued through the sixth month of administration. New cases appeared after the drug was stopped which led to the conclusion that although it was an excellent suppressive, it did not produce radical cure of underlying infections. Being tasteless and effective against all stages of the parasite, pyrimethamine has no peer as a suppressive agent so long as resistance, which has been reported in Malaya, East Africa and Venezuela, does not occur. In Venezuela the phenomenon did not appear until after a full year's administration. Since the parasite under suppression was pure *vivax*, this phenomenon might have been avoided if the original regimen had not been altered. Resistance occurs more often in *P. falciparum* than in *P. vivax*.

4-aminoquinolines. Chloroquine and amodiaquin are extremely efficient suppressive agents when administered on a weekly basis. They reduce parasite rates of all species dramatically, and they produce radical cure of falciparum infection. These exceptional qualities should place this group of compounds in the forefront of suppressive antimalarials. However, these drugs are extremely bitter and present a difficult problem when one tries to administer them to children. (A chloroquine resistant strain of *P. falciparum* recently has been confirmed in patients from a limited area of South America.)

8-aminoquinolines. This group of compounds, of which primaquine is the most effective and least toxic, is highly effective against gametocytes and is curative of relapsing infections. However, an inherent toxicity, especially to dark-skinned races, and the necessity for frequent administration make these compounds unsuitable as suppressive agents unless combined with another agent (see below).

Drug combinations. Quinine and pamaquine were used in combination as far back as the 1930's. Although somewhat effective, the shortcomings of each soon ruled them out. With the advent of more effective agents, the possibility of really effective combinations was more likely.

In the management of clinical malaria, especially of relapsing infections, primaquine has been given in combination with 4-aminoquinolines since about 1952. The two drugs together produce a schizontocidal, gametocyteocidal, tissue parasite-curative effect which is highly efficient.

The use of this combination in suppressive monthly doses was first tried among school children in Malaya in 1955. Following these trials, combinations of chloroquine and pyrimethamine were used in Liberia with good results. Trials in the Cameroons, at half dosage, were partially successful, but resistance developed to pyrimethamine. Recent trials against vivax under experimental conditions in this country have shown that chloroquine or amodiaquin combined with primaquine and administered once weekly gives an effective suppressive-sporontocidal-curative effect. Plans are now under way for an extensive trial of such a combination.

Drugs in salt. In 1952, Pinotti suggested combining chloroquine with ordinary cooking salt in an attempt to break transmission in the Amazon River Valley where effective residual spray operations or individual drug administration was not attainable. After determining that chloroquine was stable under conditions ordinarily encountered in the preparation of food, trials of the method were initiated and carried out successfully. Later, work in the U.S.A. by Coatney *et al.* confirmed the stability of chloroquine under conditions of storage, shipping, and food preparation, and showed the same to be true for pyrimethamine. Studies employing inmate volunteers showed that either of these drugs, when combined with household salt in appropriate amounts, resulted in complete suppression of vivax malaria under repeated infection by mosquito bite. Programs employing the salt-drug method are now under way in Brazil, British Guiana, Ghana, and Cambodia, and are planned for other areas of the world.

Here again, we must consider the phenomenon of resistance. It is not expected to appear against chloroquine (although recent observations permit the possibility), and whether it will appear against pyrimethamine when the drug is taken daily remains to be seen. Some investigators expect it; others do not because the drug is known to be nucleo-active, and under continuous administration blood and tissue stages would be eliminated.

Treatment of individuals and small groups. Individuals suspected or found to be infected during surveillance and small groups of isolated

contacts should be given one of the efficient schizontocidal agents, preferably one of the 4-aminoquinolines, and primaquine. Such treatment will stop any possibility of transmission immediately and cure the underlying infection.

Disadvantages of chemotherapy. Even with efficient supervision of drug administration in malaria programs, one major problem has so far defied solution, namely, the administration of drugs to infants and to young children. This segment of the population is highly susceptible to infection, and, where transmission occurs in the home, often exhibits the highest parasite rate. All too often, this portion of the population is not adequately treated, and remains as the seed bed for continuing transmission. Recent studies have shown that nursing mothers who received two to three times the normal suppressive dose of pyrimethamine transferred enough of the drug in their milk to reduce and suppress parasitemia in the babies. Under ordinary dosage it is doubtful whether enough of any drug is transferred to the nursing child to suppress parasitemia.

The Panel strongly recommends continued research in this field to discover a drug or drug combination which will have a long acting effect when administered by mouth or by injection.

Drug Resistance

Drug resistance has been known since 1887 when it was first observed in bacteria. A short time later it was learned that certain of the flagellates could become adapted to normally toxic compounds but there was no serious impact on the treatment of human diseases until bacteria were shown to acquire resistance to the sulfonamides and to penicillin. Drug resistance in malaria is even more recent. No antimalarial drug in general use during World War II was known to provoke appreciable resistance. Shortly thereafter, parasite adaptation to proguanil, stable enough to pass through the mosquito, appeared in *P. falciparum* and *P. vivax* and, for the first time, drug resistance became a problem in the management and control of malaria.

Selectivity. All malaria drugs are selective in their action in the sense that the parasite is not affected in all phases of its life cycle. Sporozoites resist any adverse action from all known drugs, and tissue stages are sensitive to only a few. The asexual parasites are sensitive to most of the accepted compounds while gametocytes are affected by some drugs but not by others. This selective natural resistance is an innate character of the parasite and is not related to prior exposure to a drug.

Infections resulting from the same species of parasite may not respond equally well to identical treatment in different parts of the world. This dissimilarity of response has been attributed to an inherent difference within a particular geographical strain. Just what is responsible for this difference is not known. It could be that geographical isolation has produced a variant with auxiliary metabolic pathways not affected by the drug. Whatever the true explanation may be, the fact remains that such strains exist in nature.

Acquired resistance is always associated with previous experience with a particular compound and hence is an adaptive change. Drug resistance has not become a formidable problem in malaria eradication because, in practice, the appearance of resistance has been limited to two drugs, proguanil and pyrimethamine.

Extent. Widespread resistance to proguanil has been observed for all species of the parasite since resistance was first recognized in Malaya in 1948. Malayan strains of *falciparum* sensitive to single small doses of proguanil in 1947 became resistant to very large doses only two years later. A thousandfold resistance to proguanil has been produced experimentally against the Chesson strain of *Plasmodium vivax*. The phenomenon extends to both asexual and sexual parasites, and the character is transmitted unaltered through the mosquito. The experience is so widespread that proguanil cannot be recommended in eradication programs.

Resistance to pyrimethamine was first recognized during trials in Kenya in 1954. It has later appeared in Tanganyika, Nigeria, and the North Cameroons, and more recently in Venezuela. At the same time, it should be pointed out that the drug has been used extensively in widely separated areas (Liberia, Morocco, Kenya, and South Vietnam) with no evidence of resistance. Resistance to pyrimethamine has been produced experimentally in strains of *P. vivax*, *P. malariae*, and *P. falciparum* and transmitted through the mosquito without loss of virulence. These results leave little doubt that resistance to pyrimethamine can develop easily under certain conditions with certain strains. Pyrimethamine has many sterling qualities and can be recommended for

selected areas under continuing observation. Strains resistant to proguanil or to pyrimethamine respond well to chloroquine. (Chloroquine resistance was first seen in mid-1960 in patients from Colombia, S.A., infected with *P. falciparum*. This phenomenon has been encountered more recently in a mild form in Venezuela. Whether resistance to chloroquine will appear in other parts of the world remains to be seen.)

Acquired resistance. Acquired resistance to quinine, quinacrine, the 4-aminoquinolines and the 8-aminoquinolines has never been demonstrated in the field. The evidence obtained from the study of experimental malaria in animals is somewhat equivocal. It appears likely that resistance to any drug should be accepted as a possibility but that the odds against the actual development of a high degree of resistance vary tremendously with the drug, being quite high with quinine, quinacrine, the 4-aminoquinolines and the 8-aminoquinolines. However, a strain of *Plasmodium berghei* (rodent malaria) obtained during a period of 7 months of treatment with chloroquine showed a 200-fold increase in resistance. With this exception the highest increase in resistance among these drugs was a 4-fold change obtained in *Plasmodium knowlesi* (monkey malaria) treated with pamaquine. The mature gametocytes of *falciparum* are naturally resistant to the first three compounds, but this poses no real problem because regular drug administration will prevent the maturing of new forms and the old ones will soon die out. As a consequence, this factor is not a deterrent to the use of these compounds in eradication programs.

In spite of the limited appearance of drug resistance up to the present, the potential for the appearance of additional difficulties must not be overlooked in the face of the general biological principle of adaptation; those responsible for drug programs must be cognizant of the general principles of the development of resistance and alert to indications of its occurrence, spread, stability, cross-resistance, and prevention.

5. ORGANIZATION AND ADMINISTRATION

There is no technical reason why malaria eradication cannot be accomplished in any part of the world with the insecticides, drugs, equipment and techniques now available.

Adaptation of the Standard Eradication Program to Local Conditions

The standard malaria eradication program—one-year preparation, four-year attack and three-year surveillance—is not suitable for all countries. It must be modified for each particular country in accord with the habits of the vector, the climate and geography of the country, the habits and distribution of the population and the logistical problems found.

These adaptations to local conditions should be made, if possible, before a program is initiated, after analysis of the results of previous malaria control programs and comparison with other eradication campaigns operating under similar circumstances.

In some cases it may be necessary, in certain large countries, to phase the initiation of eradication operations. In such cases operations should be as large as possible in the first year and be extended throughout the country as rapidly as possible.

Role and Importance of Organization and Administration

Malaria eradication involves the large-scale application of a few relatively simple procedures which have a scientific basis involving extremely intricate biological processes. Success depends on the thoroughness with which these procedures are carried out. Eradication demands precision; it cannot be achieved by slipshod methods, inadequate coverage or poorly trained and inefficient personnel.

It is impossible to transform a control program to eradication simply by extending an inadequate operation to a wider area. Eradication requires a new and far more exacting administrative approach; the organization, training, operation and supervision must all be established with the complete coverage demanded by eradication in mind, and anything less than this will mean failure.

Unfortunately, many of the areas where malaria is now a problem are areas where the authorities have had little experience in the application of modern scientific methods; they therefore lack both the scientific background and administrative experience essential to success. Although the short-term intensive training of individuals to carry out special routine opera-

tions can be highly effective, the direction of an eradication campaign needs a degree of flexibility which cannot be improvised, but comes only from training and experience. It is essential that certain countries be assisted by international technical and administrative personnel to guide operations until such time as nationals have had the scientific training and administrative experience needed to carry on without minimal international assistance.

Governments which entrust the planning and direction of eradication projects to international organizations or to ICA are entitled to the services of capable and effective personnel; experience has shown repeatedly that when an eradication program fails, its failure is more likely to be due to a lack of preparation or organization, or to some fault in the administrative machinery, than to technical reasons.

Eradication must have the full backing and enthusiastic co-operation of the national government, in developing an organization capable of doing the job with ability to employ the qualified key staff needed to carry out the program. Only thus can a country succeed in malaria eradication, realizing from the outset that partial success is failure. There is no shortcut to its accomplishment.

As each country now committed to malaria eradication is freed of infection, the international demand for the elimination of remaining sources of reinfection should become too strong for any country to resist.

Participation of International Agencies

The relationship of each national eradication service to the international agencies, PAHO, WHO, and UNICEF, and to ICA, must from the outset be clearly defined and spelled out as to financial responsibility and responsibility for technical assistance, approval of plans, selection and exact responsibilities of personnel, and assistance in continuing evaluation of results.

Planning and Preparation

Eradication calls for: (1) a carefully worked-out plan covering the entire area in which transmission occurs; (2) an administrative organization, capable of carrying out this plan; (3) suitable legislation and regulations; (4) budget planning covering the operation as a whole for a period of years; (5) effective support from all branches of government; (6) co-operation with all medical and health bodies, official and private; and (7) education of the general public.

Techniques. Within the over-all program, detailed plans should be developed covering the epidemiological and operational phases. Plans should be specific and contain estimates of needed equipment and materials, personnel, and transport for the projected period of operations.

Mapping. Accurate maps are a key factor in the planning of eradication. Large-scale maps are essential for the delimitation of malarious areas, for showing the exact location of each house to be sprayed and for the fixing of individual responsibility of field employees within definite sectors. Maps are essential at every step of the program—over-all phasing, planning and checking daily operations whether these be epidemiological or operational.

Timetable. The general pattern of the standard eradication program (preparatory, attack, consolidation and maintenance) which must be modified and adapted as the program develops, may be outlined as:

a. *Preparatory phase:* an initial malaria survey and preliminary spraying operations in pilot training areas; planning; necessary legislation obtained; equipment and material stockpiled; personnel hired and trained. This preliminary phase may require a year or more, depending on previous control operations and availability of data and personnel.

b. *Attack phase:* four years of active spraying with results continuously checked by epidemiological evaluation, to insure complete cessation of malaria transmission and the emptying of the parasite reservoir in the human host.

c. *Consolidation phase:* three years devoted to an active search for residual foci of transmission. Epidemiological evaluation continues as part of surveillance, when the fact of eradication is being confirmed.

d. *Maintenance phase:* begins when eradication has been achieved and continues as a function of the health department as long as malaria exists elsewhere in the world. The disease remains notifiable, and any imported or introduced cases must be dealt with adequately by the health department. Those planning the program should

make provision for the continuing action of the health department.

Organization

National government and governmental agencies. The eradication service must be an integral part of the governmental structure, with the necessary backing from the government to insure its success. The eradication service is normally planned as a special temporary service established to accomplish a definite mission within a limited period.

Provision should be made in the regulations for financial and accounting procedures to permit the uninterrupted flexibility of action needed for operations on a shifting front. International participation generally requires special regulations (for example, delegation of authority as regards financial and personnel matters), and special privileges as regards taxes, salary scale, budget, import duties and administrative matters. The eradication service will in some instances temporarily overlap or replace the work of other agencies. This requires acknowledgment by the government of the importance of the program and the acceptance of responsibility for establishing working arrangements with the other government agencies concerned. Co-operation with these agencies is essential and must be assured. Rivalry or opposition can seriously jeopardize the all-out effort needed for success.

Organization of national malaria eradication service. Malaria eradication programs should be directed by a special malaria service, preferably a primary division of the national health department, with a national malaria council to advise on general management and to coordinate malaria activities with those of other services.

The eradication program should be developed along two main lines: epidemiological and operational. The administrative structure will depend upon the size of the population to be served, preferably with centralized direction and decentralized execution. The epidemiological service should outline the malarious area and establish the definite boundaries of the area to be worked. From the beginning, epidemiological studies should be maintained to determine the places where transmission still continues, and to indicate when spraying can be discontinued in cleared areas.

After a detailed ground study of the number of houses in each locality, and the ways and means of transportation, the field services should draw up the itineraries of work to be followed by the spraying squads and indicate the geographical limits of each squad's responsibility.

Legislation. For the proper implementation of a malaria eradication program, pertinent national regulations are generally necessary, the nature of which varies with the situation in each country and with existing legislation. The regulations should cover, with sufficient clarity to avoid any argument, the following:

(1) Definition of the nature of the problem and the methods to be employed, including priorities for various sections of the program and areas involved;

(2) Provision of an adequate and stable budget for the complete program of eradication, with provision for an adequate reserve fund to guarantee regular monthly payment of salaries and operating costs;

(3) Nature of personnel required for treatment, laboratory diagnostic work, surveillance and administration, their duties, salaries, privileges and obligations;

(4) Obligations of the public as regards collaboration with survey and eradication personnel, in connection with entry and spraying of all habitations, and medical examination of individuals;

(5) Compulsory notification of suspected or confirmed cases; malaria should be classified as one of the nationally-reportable diseases and should be subject to the appropriate rules and regulations, which should be enforced by law and which may, under special conditions, include quarantine measures;

(6) Special measures for the prevention of reinfection, including quarantine regulations governing the movement of populations from malarious areas to areas free from the disease;

(7) Remuneration of those responsible for the execution and observance of the law, and determination of penalties and awards.

Provisions should be made for legal help in interpretation of the malaria regulations and in dealing with other agencies and the public. The service may have to apply legal sanctions on occasion and may in turn be subject to damage suits or injunctions.

Recruitment and Training

Basic staff needs must be carefully estimated in the planning stage; these comprise field workers

for spraying operations and for epidemiological evaluation (including medical, entomological, engineering, educational and administrative disciplines) and a special headquarters staff in epidemiology, entomology, engineering and health education, as well as an effective coordinating administrative staff.

Director. The national director should be a person with prestige in his own country and with the confidence of the government. He may be drawn from almost any discipline, but must have leadership qualities as well as administrative ability and special knowledge in the field of malaria eradication. Qualities of administrative ability or knowledge of malaria eradication are also essential in his principal assistants.

Key personnel. In countries of about a million population or less, the national organization is primarily one of field operations in spraying and epidemiological evaluation, assuming that specialist guidance in entomology and other special fields can be supplied by co-operating agencies. In large countries full time local specialists should be employed. Sometimes they are readily available, as in India; sometimes they must be trained. The staff of highly specialized personnel need not be large; all routine work even in special fields can be mastered by individuals of all races who have no advanced education but who can work well under supervision.

It has been assumed, at times, that the only measure of proper spraying is the epidemiological one, namely, the decrease and final disappearance of malaria. This measure has been applied relatively late in the campaign, often after years of effort have been lost because of uncorrected deficiencies. Spraying itself has standards of performance which should be applied by adequately trained personnel as a measure of success before the epidemiological results become apparent. The key personnel are at three levels of supervision: (1) the headman directly in charge of a spraying squad; (2) the supervisor of a group of spraying squads, often called a sector chief; and (3) the supervisor covering several sectors at the zone level.

A zone of about a million people is large enough to carry on operations with considerable administrative autonomy, but it must have a capable administrative chief. In a large country, supervisory personnel above the levels indicated cannot have personal knowledge of all local operating conditions. If sectors are too large, with insufficient supervision by the zone office, there will be inadequate checking of the coverage of all houses and of all pertinent parts of each house. To insure the interruption of malaria transmission it is important that close to 100% of houses be adequately sprayed. Sufficient personnel should be supplied at the supervisory levels to insure this result. If sanitary inspectors are available they should be used; if not, the most intelligent and active sprayman will have to be trained as supervisors.

Personnel for a population of one million. As the number of cycles per year is increased or the seasonal period of spraying shortened, the personnel needs are increased almost in proportion. By conservative estimates, the personnel required for a total population of one million in a continuous 12-month spraying cycle are 100 spraymen, 20 headmen, 10 sector chiefs, and 5 zone supervisors; two-cycle (6-month) continuous spraying requires 200 spraymen, 40 headmen, 18 sector chiefs, and 8 zone supervisors; and the corresponding requirements for two-cycle spraying for 2 months only are 600, 120, 30, and 12.

The selection of qualified individuals for headmen and supervisors at the sector and zone levels is of the greatest importance. Effort should be made to work out a plan to keep them continuously employed, with a government career open to them as long as they perform efficiently.

Personnel for evaluation. A large personnel is also required for the epidemiological evaluation service. Estimates have been made of one evaluator to 10,000 population, or as many as there are spraymen in a continuous one cycle operation. These evaluators should be of a category equal to that of spraying operation headmen and, if possible, recruited from that staff. As high a number as this might be expected where a very active search for cases was contemplated (such as a house-to-house survey repeated every two weeks), an expensive procedure. Wherever local collaborators do the bulk of the evaluation, under careful supervision, supplemented by selective area surveys and spot checking, a much lower number would be required.

Entomologists. Special attention should be given in each country to the need for an adequate number of entomologists and to the training of entomological aides.

Recruitment. Great difficulty may come in recruiting personnel for the eradication service because of existing merit systems, which may have

educational standards that cannot be readily met. There should be flexibility in this matter, loan of maximum number of qualified individuals from other services should be made, and arrangements made for training of new personnel. This training need not be unduly time-consuming, because one of the great advantages of eradication programs is that they are based so largely on routine activity of nonprofessional and relatively untrained staff which can be taught to do routine operations efficiently under supervision. The success or failure of the eradication program will depend largely on the efficiency of the spraying operations, and it is here that the largest number of personnel are needed.

Training. Training of all but key national personnel will have to be provided almost entirely within each country. Consideration should be given primarily to the training of spraymen, headmen, sector and zone supervisors. Spraymen can be adequately prepared in a two-week intensive training course with a variable period of practical experience; headmen will probably require an additional week; at higher levels, a six-to-eight week course will be needed to make them competent to supervise the activities of spraymen and headmen. Instruction for this latter group should include, for example, more about the disease itself, its detection by blood smears, the use of the common antimalarial drugs, and the maintaining of good public relations. Again, it is emphasized that large numbers of these individuals are needed early and continuously throughout the spraying operation. By the establishment of one or more small training units, large numbers of this important group can be trained and given practical experience.

Since the greater portion of this training is of a practical nature, the use of audio-visual aids as well as actual spraying equipment is most helpful. Basic material can easily be prepared in any local language required.

The recruitment of experienced malariologists and other specialists is difficult because of a limited supply.

Malaria eradication training centers established in Jamaica, the Philippines, and elsewhere will continue to give basic orientation to those physicians, entomologists, and engineers who can be recruited for eradication programs; they should be reserved for men who have had little previous experience in this work. A 10- to 12-week period seems to be adequate for this basic training, and a month of careful observation of a successful program elsewhere would seem to be sufficient preparation for these men to begin working under supervision in actual programs.

There are officials in many countries, directly or indirectly involved in malaria eradication programs, who cannot be expected to profit from a detailed, intensive course but who would receive orientation and stimulus to do a better job by visiting successful programs in other countries. Part of the value is in seeing programs, part in meeting and talking to men who are recognized as authorities. There are programs where much can be learned. Training visits are best limited to one or two countries. The assignment of a qualified coordinator of these visits in countries where field observations are to be made is especially helpful, and provision should be made for interpreters when necessary.

A basic principle in the training plan should be training from the top down—having key people train supervisors, who in turn train the field staff. Essential to the success of an eradication program are the care and thoroughness with which each supervisor checks, rechecks and double-checks the performance of each subordinate, from the program chief all the way down to the sprayman in the field.

Finance

Lack of adequate provision for financing has been a major handicap to many eradication projects. Interruption of an eradication campaign is critical, since this can jeopardize the entire program. Until a project is successfully completed it can be set back either partially or completely by interruptions; it is unique in this respect. Achievement of eradication requires that particular care be given to assure that the necessary funds be made available uninterruptedly throughout the entire program, and that funds be allocated to the malaria service without being hampered by delays entailed in the routine reviewing of individual expenditures.

Logistics

Eradication, in contrast to a control program, depends on the effectiveness with which the organization can get men and materials to even the most isolated areas at the right time. This often involves long lines of communication over difficult terrain and under poor living conditions.

Problems of transport, of supply depots, of men living and working away from home, of overtime and subsistence allowances, of repair facilities, and others become major issues.

Transport. No general rules can be established for transport requirements except that wherever possible, reliable local services should be utilized. Pack animals, boats and sometimes bicycles can be procured locally; jeeps, landrovers and trucks may have to be imported.

Supplies and equipment. A detailed list of equipment and supplies, subdivided into needs with respect to time and location, is essential. This is particularly important in the early stages of planning operations if much of the equipment and supplies are procured outside the country. Procurement must be given ample consideration in planning. Wherever possible, local sources of supply or manufacture should be used.

Warehousing, garage, repair facilities. Adequate warehousing and garage and repair facilities must be available, together with a proved system of issue, use and repair. Lacking a tested control system, advantage may be taken of military experience for this purpose. The rules and regulations which are established should be made available in manual form and distributed to all personnel concerned.

Health Education

Emphasis has been placed elsewhere on the importance of adapting malaria eradication operations to the biological behavior of the local anopheline vector. It is equally important to adapt to the mores and behavior of the human population and especially important to recognize the necessity of teaching all levels of society the objectives of the malaria eradication program, the reasons for the techniques used and the overall long-time advantages for the entire population. Individuals, acting as budgetary or legislative authorities, determine the amount of money to be spent on malaria eradication; other individuals, in the finance and health ministries, decide on the timing and orientation of the program. Still other individuals must give counsel on the technical and administrative details required for eradication. However, in the end, success depends on getting the full-hearted co-operation of the householder and especially of the housewife, in gaining entry to the home for the spraying of insecticide, in taking blood slides for evaluation of progress, and in the reporting of fever cases and the administration of drugs.

Effective education at all levels is essential to intelligent decision and continuing collaboration until malaria is no more. The widespread dissemination of information alone does not guarantee conviction and favorable action. The malaria eradicationist must be ready to adapt his teaching methods to the social, cultural and educational background of the population living in the malarious areas to be cleared of the disease.

There is no one right or easy way to get people interested in malaria eradication and ready to collaborate fully. Many different educational approaches are needed.

Plans should include especially the appropriate education (in the meaning and method of malaria eradication) of national and local officials, doctors, health officers, para-medical personnel, practitioners of indigenous medicine and midwifery, and most certainly, the staff of the malaria eradication project at all levels, particularly the spraymen.

The educational part of the malaria eradication program should be planned from the beginning and in as much detail as any other part.

In many countries with malaria eradication programs, the necessity of educating the people has not been given sufficient attention. This is shown by resistance to insecticidal spraying by a significant percentage of the householders. Considerable time is lost on repeat visits to homes which could not be sprayed on the first visit. Resistance to blood sampling and to continued drug treatment is reported. Resistance is often due to apathy, to lack of information, to misinformation, to disappointment over failure of previous spraying to kill all household pests and to fear of the poisonous effects of insecticides.

These problems of human resistance are apt to continue and multiply unless educational plans, each adaptable to the situation in a given area, are developed and carried out. In each country, the problem must be identified and the appropriate educational treatment determined. The persons to participate in the educational program must be selected and trained in accord with a planned procedure with adequate staff and budget.

The task of learning why people react unfavorably to malaria eradication and how to induce a favorable reaction is difficult. Placing health education specialists on the malaria staff is recommended. Although some countries have

competent directors and staff of health education, these persons are usually over-loaded with other work and rarely has any one of them devoted full time to malaria eradication.

Need for health educators. ICA and PAHO/WHO health education advisors both recommend that health educators be employed in malaria eradication programs. They have prepared a bulletin entitled "Educational Approaches in Malaria Eradication" and distributed it in draft form for comment to malaria health educators throughout the world. The final draft of the bulletin should be ready for publication in the near future.

At the present stage of health education in many countries with malaria eradication problems, outside assistance is necessary, but local budgets must provide for national health education staff and for the production of teaching materials. Once the plan for teaching the people has been drawn up, this national education staff must in turn orient the rest of the staff of the eradication service on how to get the necessary ideas across to the people, to guarantee their individual and collective community support of the program.

Lack of funds and personnel, political instability, slow and difficult transportation, language differences within a country, illiteracy—all these are barriers which make the educational task in malaria eradication difficult and complex. However, an understanding and application of a few basic principles of how people learn and how their support can be gotten will do much to strengthen the malaria eradication program.

The educational problem must be solved if the goal of eradication is to be achieved.

6. COST OF GLOBAL ERADICATION

The Panel has considered estimates prepared by WHO, PAHO and ICA of the total resources needed for the completion of the world-wide malaria eradication program. These estimates, covering whatever period of years may be required for final success in a large number of diverse countries with varying operating conditions, subject at times to political changes, cannot have the degree of precision expected of annual national budget estimates. The estimates do, however, serve to focus attention on the general magnitude of the effort that infected countries, international organizations and supporting governments must make to assure success (Table 4).

Unlike the Malaria Report of the International Development Advisory Board (IDAB) made in 1956, which attempted to outline costs of a limited effort during a five-year period (excluding all of Africa, the Amazon Valley of South America and a number of highly malarious areas in other parts of the world), the Panel attempted to project the cost of completing world eradication with the omission only of Mainland China and a few other territories for which data are lacking.

Cost Estimate

The cost elements have been grouped into: (1) *foreign exchange cost, i.e.*, goods and services which the malarious countries as a rule have to import from abroad, such as insecticides, spraying and transport equipment, microscopes and advisory services; and (2) *local currency cost, i.e.*, payments for labor, administrative services, and incidental goods that the malarious countries have available in their own economies. Where outside assistance is given it usually refers to the whole or to a part of the foreign exchange cost.

Foreign exchange cost. As regards the estimate of foreign exchange costs, the Panel has followed the WHO unit-cost method (see WHO Document PA/12.6 of 29 January 1960); details of the calculations are set forth in Table 5.

In conformity with its recommendation regarding the required dosage of insecticide (per unit of sprayed surface), the Panel has based its estimates of the cost of insecticides on the assumption that its recommended reduced dosage will be used in most countries. The present estimate, therefore, is based on the arbitrary assumption of using 2 g/m² of DDT in the countries of the Americas (where this dosage is being generally used in well advanced programs) and 1 g/m² in other regions. Future experience will be needed to arrive at a realistic geographical pattern of dosage distribution in conformity with the scientific, physical, political and administrative factors that will determine the final decisions in this matter.

Local currency cost. As regards the estimates of local currency costs, the Panel has considered the cost experience of countries for which records are available as well as certain forecasts made by various authorities in the field. In general, local currency costs expressed in dollars tend to be twice as large as foreign exchange costs, with the notable exception of India where, owing to special circumstances such as the high concentration of population and home production of a

TABLE 4

Some estimated costs of malaria eradication from 1960 to end of program

World regions	Population (in millions)	Foreign exchange cost (in millions*)	Local currency cost	Total cost
Far East.....	154.1	82.5	198.0	280.5
Near East and South Asia..	517.1	133.6	358.8	492.4
Africa.....	187.9	117.8	282.7	400.5
Latin America.	84.8	50.7	101.4	152.1
Europe.....	19.3	5.0	12.0	17.0
	963.2	389.6	952.9	1,342.5

* Expressed in U. S. dollars.

certain amount of DDT and some equipment, local currency cost tends to be three times as large as foreign exchange cost. The factor of three to one for India is true only if the entire period of eradication is considered. During the tooling-up period and during the attack phase, when large amounts of DDT are being used, foreign exchange cost is high, whereas local costs predominate during surveillance. In cases where no information is available, *e.g.*, for African countries, the Panel has computed local currency costs by multiplying the estimated foreign exchange cost by a factor of 2.4, which reflects the effect of a reduced dosage of insecticides.

The cost estimates contain far-reaching implicit assumptions pertaining to administrative efficiency, monetary stability, and the development of insecticide resistance. Furthermore, technological innovations would naturally create an entirely new cost picture.

Total cost. The total cost of global eradication has been summarized in Table 4; it can be seen that the eradication of malaria from the presently malarious non-communist countries and territories, comprising a total exposed population of about 960 million people, will require foreign exchange expenditures of approximately $390 million and local currency expenditures of approximately $950 million, or a total expenditure in excess of $1.3 billion during the period beginning with calendar year 1960. Included in these figures are the costs of completing the programs already under way as well as the full cost of programs still to be initiated.

The above estimates represent minimum cost, and are expressed in terms of dollars of present purchasing power, following basic procedures currently used in the conduct of eradication programs. They do not allow for the great number of technical and administrative contingencies which prudence requires to be taken into account. Not less than 50% in the case of

TABLE 5

*Foreign currency cost**

Program year	DDT		Sprayers and parts	Vehicles and parts	Drugs	Microscopes	Advisory services and hqs. costs	Total	
	1 cycle† 1 gram	2 cycles‡ 2 grams						1 cycle 1 gram	2 cycles 2 grams
Survey				7.5				7.5	7.5
Preparatory	3.7§	7.5§	1.6	.8	.2	.3	1.0	7.6	11.4
Attack 1	3.7	7.5	.6	.8	.3		1.0	6.4	10.2
Attack 2	3.7	7.5	.6	.8	.4		1.0	6.5	10.3
Attack 3	3.7	7.5	.6	.8	.5		1.0	6.6	10.4
Attack 4	3.7	7.5	.6	2.6	.5		1.0	8.4	12.2
Consolidation 1				2.6	.5		.2	3.3	3.3
Consolidation 2				2.6	.5		.2	3.3	3.3
								49.6¢	68.6¢

* Unit cost per head expressed in U. S. cents.

† A cycle represents one spraying a year.

‡ Assumes that each cycle is completed in six months if two cycles are used.

§ The small errors involved in neglecting further decimals are partially compensated by calculating 1 gram at 3.7¢ and 2 grams at 7.5¢.

total cost, and not less than 25% in the case of foreign exchange cost, should be permitted as an adequate safety factor in such long-term estimates. Annual revisions of such estimates on the basis of additional experience are essential.

Assumptions Made in Cost Estimate

Technical assumptions. (1) DDT water-dispersible powder will be sprayed at the rate of 1 gram technical DDT per square meter of house interior once yearly during four years of attack or 2 g/m² yearly where two sprayings are adopted; focal spraying during the consolidation years will consume the equivalent of one additional year of attack; in countries not yet in an eradication program, where transmission is perennial, two sprayings will be made; the cost of 0.5 grams of dieldrin will be equivalent to 2 g of DDT;

(2) 500 sprayers per million persons will be provided initially with allowance for nozzle tips and replacement parts; (this amounts to 1 sprayer per 2,500 population, with 400 in use and 100 in reserve);

(3) 30 vehicles per million persons will be supplied for the beginning of the preparatory year; replacement of 25% of the initial fleet of vehicles in the fourth year of attack and the 2 succeeding years will be provided or substitution made of other type of vehicle suitable for the consolidation phase depending upon local needs; in each year after the first, 10% of the purchase price will be required for replacement parts for each vehicle;

(4) Drugs will be provided on an increasing scale from the first through the fourth year of attack to facilitate the collection of blood slides from fever cases for diagnostic purposes (second year consumption increase, 50%; third year, 100%; fourth and subsequent years, 150% over that of the first year); drug consumption will continue at the fourth year rate through the 3-year consolidation phase;

(5) For the last year of attack and the consolidation years, 1% of the population will be examined monthly by surveillance personnel and given single-dose treatments (adult dose, 600 mg chloroquine plus 50 mg pyrimethamine); 0.03% of the population under surveillance will, on the average, be found infected and will receive a 14-day treatment (adult treatment 1,500 mg chloroquine plus 210 mg primaquine);

(6) Ten compound oil-immersion microscopes will be provided initially for each one million population;

(7) Advisory services and headquarters backstopping will cost 1 cent per capita during the preparatory year and the 4 attack years; for the first 2 years of surveillance the cost will be .2 of a cent per capita.

Price assumptions. The cost estimate (in U.S. dollars) was based on the following average prices, which include freight and insurance: DDT 75% water-dispersible powder, $560 per metric ton; sprayers, $30 each; vehicles, $2,500 each; chloroquine tablets, 150 mg base, $6.75 per 1,000; pyrimethamine tablets, 25 mg base, $4.70 per 1,000; primaquine tablets, 15 mg base, $4.40 per 1,000; binocular microscope and lamp, $300 each.

Unit costs. The estimated unit cost of treatment (based on the above assumptions) is summarized in Table 5.

Sharing the Cost of Eradication

Since the operational initiation of the world-wide malaria eradication program in 1958, the cost of the program has been met in the main by the governments of the malarious countries, by the U.S. Government, and by WHO, UNICEF and PAHO (Table 6). The United States contributions to national malaria programs and to the special malaria funds of the Pan American Health and World Health Organizations represented 71% of the foreign exchange cost and 31% of the total cost of the world campaign; it cannot be expected that this one-sided pattern will continue at its present ratio. It is important that the common objective of world-wide malaria eradication, established by the World Health Assembly in 1955, be given financial support by the member nations in accord with their economic resources, in conformity with the high priority of the objective and the dimension of its cost.

7. EVALUATION AND MEASUREMENT OF DISAPPEARING MALARIA

Before DDT and Eradication

Before acceptance of the concept of eradication, the prevention of malaria was only partial; its reduction was usually gradual. In the earlier control programs some continuing transmission was expected. Malariologists measured the reduction of malaria from year to year, by indices of

infant infections, of blood parasitism in children and of juvenile splenic enlargement.

The index of infant infections gives a measure of continuing transmission in the homes where births have occurred during the previous 12 months, but no indication of the situation in other homes. The index of blood parasitism in children is a measure of the upward or downward trend of infection in the homes from which they come; the index of splenic enlargement in children is a gauge of a chronic reaction to malaria infection from year to year; neither is sufficiently sensitive to indicate rapidly the interruption or continuation of transmission.

During Eradication

The malariometric methods of a control program are quite inadequate for eradication, particularly as extinction is approached. An eradication program requires precise knowledge of the persistence of malaria transmission before eradication is complete, and any reappearance thereafter. Surveillance requires techniques and practices that enable the eradicationist to gauge the amount of diminishing infection remaining after apparent disappearance of the disease and to identify foci of continuing transmission.

Surveillance, an essential element of an eradication program, is defined by the World Health Organization's Expert Committee on Malaria as:

"that part of a malaria eradication project designed to discover evidence of any continuation of transmission, to establish its nature and causes, to eliminate residual foci, to prevent or cure such residual or imported malaria infections in man as would delay the ending of transmission or threaten its resumption in a given area and, finally, to substantiate the fact that eradication has been achieved." (7th Report, 1959, page 7.)

Techniques of evaluation. Epidemiological evaluation carried out during the period of residual spraying gives a clear indication of those population groups which are still exposed to infection.

Foci of malaria may be identified from (1) infant parasite rates; (2) parasite rates in children; (3) blood parasite surveys of all ages, either by sampling or mass surveys; and (4) searches for malaria infections through the systematic examination of blood smears of febrile cases. Blood smears may be collected by local health service personnel or special representatives making rapid, periodic visits. Generally it will be found practical to plan surveillance to reveal with minimum effort the places where transmission continues. This can be accomplished by utilizing the surveillance techniques known as active and passive case detection.

Active case detection utilizes traveling representatives of the eradication service. They periodically visit all homes in their districts, searching for febriles and for persons with histories of fever since the last visit. Blood smears are taken for diagnosis.

Passive case detection depends on the cooperation of persons living in the malarious villages and who are not part of the malaria eradication service. It has been termed passive since no active search for febriles is made; the system depends on ill persons visiting the fever reporting post where blood smears are made for diagnosis and antimalarial drugs are provided. A network of fever reporting posts may be established utilizing the services of local physicians, health centers, and hospitals or lay collaborators appropriately trained for the task.

In some countries effective case finding is being achieved by the use of the lay collaborators. Careful selection of these individuals is essential to the success of the system. Local individuals should be chosen who are in close contact with the people whose confidence they possess. The collaborators are trained to make blood smears, to dispense antimalarial drugs and, in some instances, to act as epidemiological aides. Each collaborator provides antimalarial drugs to each fever patient to stimulate the reporting of fever cases and to render malaria cases non-infective.

Passive case detection will not be effective unless the malaria service actively recruits, stimulates, visits and checks the work of local resident representatives. One great advantage of the local medical and lay collaborators who serve in passive surveillance is their close, permanent contact with the local population.

Measurement of disappearing malaria. The Panel was concerned by the high cost of active surveillance, but recognized that if new infections are to be discovered, diagnosed and medicated before becoming infective for the mosquito vectors this activity is essential. As the incidence of malaria decreases, it is probable that the less costly passive surveillance may become relatively

TABLE 6

Source of funds for malaria eradication 1958–1959–1960 (in terms of thousands of U. S. dollars)

Agency	1958 (actual)	1959 (actual)	1960 (estimated)	Total
WHO	4,563	4,940	6,841	16,344
U. N. technical assistance	787	762	664	2,213
PAHO	1,886	2,900	3,450	8,236
UNICEF	8,700	8,300	10,000	27,000
U. S. bilateral*	20,240	20,205	27,000	67,445
Countries with malaria	54,600	50,800	54,600	160,000
Total	90,776	87,907	102,555	281,238
Foreign exchange component of total expenditure	36,176	37,107	47,955	121,238

* In addition to its bilateral aid in malaria eradication, during the calendar years 1957 through 1959, the United States contributed 7.5 million dollars to the PAHO and 11.0 million to the WHO Special Malaria Eradication accounts.

less productive since the number of slides from fever cases will be out of reasonable proportion to the number of infections found.

Although the infant parasite rate and the parasite rate in children are useful indices in epidemiological evaluation in static populations in the early phases of eradication, they are quite inadequate for evaluation among such mobile fringe populations as lumbermen, fishermen, charcoal burners, and chicle gatherers, and among seasonally isolated farm workers, who become extremely important in the consolidation period. In the latter phase, all infections are equally dangerous and significant. It seems probable, therefore, that more reliance will be placed on systematic blood parasite studies. These will reveal foci of transmission if based on repeated sampling of special groups shown by previous investigation to be the most exposed.

The great difficulty in the final stages of disappearing malaria is to reveal any malaria transmission. At this point, parasite carriers, with or without symptoms, must be found. Each individual found positive by blood examination should be subjected to epidemiological inquiry to determine the place and time of infection to aid in classifying it as a new case, a relapse, a transfusion infection or an introduced case.

The inquiry should be made by a qualified epidemiologist or by an aide who can make blood smears and obtain information concerning the probable time and place of infection. The parasite-positive individual is queried and the information obtained is recorded on standard forms and becomes a part of the permanent, cumulative epidemiological file of the area. The field investigation should be extended to include members of the family and neighbors. A blood smear is taken and reports completed for persons with histories of febrile attack.

On the basis of this history the epidemiologist classifies each case. The location of the place where transmission was presumed to have occurred is spotted on the map by appropriate time interval, to relate, if possible, to other cases in time and space.

The Panel suggests that additional study is needed to determine the best means of identifying cases under various epidemiological conditions. Flexibility in modifying surveillance in accord with available epidemiological information is essential to avoid unnecessary expenditures in areas where malaria transmission has ceased.

Management of disappearing malaria. In some programs attempts are being made to identify individual infections as soon as they occur and to give suppressive treatment before the individual becomes infective for mosquitoes. Active case finding is being carried out with surveillance agents visiting villages every 2, 3 or 4 weeks.

In areas where transmission has ceased, the finding of each imported infection is necessary to prevent transmission. In areas where active transmission exists, it is obvious that it cannot be blocked readily by identifying and treating individual cases. The finding of one or more locally acquired cases, therefore, may require the blanketing of the locality rather than the treatment of cases. It may necessitate spraying the entire area of the suspected focus of transmission or mass treatment of the population involved. In choosing the method to be used, it must be remembered that in spraying the unit of control is the house, in therapy it is the individual, always more difficult to find and to treat.

Training of Evaluators

Since surveillance is as indispensable in malaria eradication as are administration and operations,

provision should be made for the recruitment and training of epidemiological evaluation personnel in the early phases of the eradication program. It must be borne in mind also that health education of the public is just as essential to the success of surveillance as it is to spraying operations. The director of the surveillance team should be a well-trained epidemiologist, the optimum being a medical graduate with public health education and experience in administration and epidemiology; he should be sufficiently familiar with the tasks of all his subordinates to be able adequately to supervise their training and their work.

The first echelon of these will consist of epidemiological assistants, prepared to take charge of surveillance operations in individual sectors of the eradication area. It is desirable but not essential that the assistant epidemiologists be medical graduates; they should have a public health background, administrative ability and a sound appreciation of effective public and professional relations, as they will be dealing with local physicians and residents.

Next in order are the epidemiological aides, trainable lay collaborators who can read and write. Their supervisors will help them make friendly contact with the residents of their areas, to whom they should explain enough of the eradication mission and operations to secure local co-operation. These aides should be honest, careful, and intelligent. They must be shown how to make thick and thin blood films, how to use clinical thermometers, how to perceive circumstances which may relate to the success of malaria eradication from the standpoint of popular co-operation, how to interrogate skilfully to gather the information desired, and how to keep accurate records. They may also be used under certain circumstances for the distribution of antimalarial medication. Their number will vary with the size of the operational area, the distribution and accessibility of its population, and facilities for transportation and communication. But under no circumstances should a lay collaborator be assigned a sub-sector too extensive, populous or difficult of access for reliable surveillance by one individual. Too heavy an assignment is poor economy, since the future maintenance of malaria eradication must be based on the information he supplies.

There must be effective administrative procedures for translating the epidemiological findings of surveillance into prompt remedial action if required. Expeditious reporting, quick analysis and immediate action are all imperative if surveillance is to carry out its key functions in a malaria eradication program.

Certification of Eradication

If surveillance is effectively practiced and maintained, geographically and temporally related cases of malaria will be found as long as transmission continues. When transmission is stopped owing to vector control, seasonal changes or other causes, the number of cases will diminish rapidly, *i.e.*, malaria will tend to disappear, and the residual cases will consist of sporadic and unrelated instances of introduced or relapsing infections. When surveillance over a period of three years—during at least the last two of which no vector control or mass medication programs are carried on—fails to reveal primary, indigenous cases in a particular region, *malaria eradication* may be claimed, in accordance with the criteria of the World Health Organization.

8. MALARIA ERADICATION AND POLITICAL PROBLEMS

There are political as well as administrative and technical obstacles to malaria eradication. They may be caused by political action—or inaction—or may arise from difficulties based on unfriendly relations between governments. Such obstacles, not susceptible to administrative correction, may have to be solved through diplomatic channels where bilateral aid is involved, or through international parley.

Oftentimes the answer lies in health education of a high order, directed particularly at top national and provincial levels. The solution is facilitated when officials at those levels realize the political assets that can accrue from being identified in their own country with the achievement of malaria eradication.

Problems of this nature are neither isolated nor unique and may occur during any phase of the eradication program. Failure to solve them in one country may not only interfere with the progress of the campaign in that country, but may increase costs and delay the attainment of eradication in adjacent countries. These problems must be faced as soon as they are detected, and remedial action sought.

Problems of a political nature that affect specific eradication programs, fall into the following

categories: (1) recalcitrance of local inhabitants opposed generally to government activity; (2) relegation of malaria eradication to low priority in competition for available financial and personnel resources; (3) political appointees unqualified or uninterested in malaria eradication; (4) conflict of national interests of contiguous malarious countries, making coordination of eradication programs difficult; (5) civil insurrection or rebellion; and (6) non-participation of the governments of certain malarious countries in international organizations sponsoring malaria eradication.

Recalcitrance of Local Inhabitants

There are countries in which the reluctance of spraying teams to enter malarious areas inhabited by unfriendly tribesmen has prevented complete national coverage. In some countries there exist undeveloped areas, remote and difficult of access, inhabited by primitive peoples who have had little contact with civilization and prefer even less.

These problems offer a challenge both to logistics and to the health educator. Transport problems have sometimes been met even by air-drop. The challenge of unfriendly, *i.e.*, ignorant, populations has at times been met by dedicated individuals and government personnel who have contrived to make the hostile population aware of the benefits of eradication. Several graphic examples could be cited to show that primitive people can be made completely responsive to public health programs, that they are just as desirous as are more advanced populations to be rid of disease, once they are made aware that disease is not inevitable, that it can be prevented.

Relegation of Malaria Eradication to Low Priority

The priority given to malaria eradication is based, all too often, on a political decision with adverse economic and health consequences. It is understandably difficult to maintain a high priority for eradication in a country where malaria is not a primary or major public health problem. In other circumstances, low priority may be given because the problem is believed to be insoluble and any resources devoted to it wasted.

The matter of priorities may also be involved where governments—or regimes—change, or where one political party is succeeded by another. It does not necessarily follow, however, that changes in governments will change a high priority already given to a malaria eradication service, particularly if the program enjoys enthusiastic popular support.

In several instances the decision to give malaria eradication a low priority has been reversed as a result of friendly representations and offers of co-operation from neighboring countries motivated by enlightened self-interest.

Here again health education—at the highest national level—may be the solution. If those in power come to realize that malaria eradication can be an important source of popularity and support by populations living in malarious areas, the program is most likely to be given its desired priority.

Unqualified or Disinterested Appointees

The staffing of a malaria eradication service is an administrative task. But staffing problems arise from time to time that may be solved only at the highest national political level—and sometimes at the international level through the friendly offices of an international organization of which the country is a member.

As has been pointed out earlier, the best solution is the selection of a first-class administrator to head the program, giving him the complete authority to hire and fire employees. Here it is well to bear in mind that in many areas of the world political appointments or those made for reasons of consanguinity are so much the accepted way of life that appeals for top-level intervention should be made only as a last resort. Such appeals should be made when it is considered that the whole eradication program is jeopardized by ill-advised political or nepotistic appointments, and that the incumbent is not amenable to adequate training or the instilling of enthusiasm for eradication.

Conflict of Interests of Contiguous Countries

Ideally, national borders should not unduly influence or limit malaria eradication. Physical, epidemiological, topographic and demographic considerations should determine the area and timing of eradication measures. However, adjoining countries may give different priorities to eradication within their boundaries, and border areas across which transmission may occur become important. There are cases in which a well-

conducted program in one country is threatened by a neighboring country that is negligent in the operation of its program. Situations such as this are sometimes remedied through diplomatic channels, through the aid of an international organization or by informal discussions between the malariologists and other public health officers of the two countries.

A practical solution may be the creation of an antimalaria coordination board, consisting of a representative of the health services of each of the countries involved, which meets with representatives of the multilateral and bilateral agencies. This procedure has met with considerable success in furtherance of useful co-operation in the malaria eradication programs of six countries in Southeast Asia and of the seven countries of Middle America. These Boards meet periodically to discuss border problems and to plan coordinated solution of common problems. In some countries informal arrangements exist permitting control teams to cross adjoining borders without interference.

Civil Insurrection or Rebellion

Several countries, because of civil insurrection, may not be able to initiate eradication programs, or have had to interrupt programs already started. In some countries there may remain areas hostile to the national government; in others, spray and surveillance teams fear to enter certain regions still occupied or subject to incursions. These situations have in the past substantially curtailed, when they have not entirely interrupted, eradication activities.

Even in the face of such situations, eradication programs have not always had to be curtailed or suspended. There are instances where agreements between hostile elements in countries disturbed by civil unrest have permitted continuation of health programs, including malaria eradication, to the benefit of all. It is a matter of good fortune when such expedient arrangements are possible.

Otherwise the program will simply have to wait until sufficient order and authority are restored to resume operations. Unfortunately, a serious interruption in the eradication program may necessitate the repetition of much, or all, of the work already done. Every attempt should be made to avoid any interruptions.

Non-participation of Governments in International Organizations Sponsoring Malaria Eradication

There are some malarious countries which currently lack political relations with neighboring countries engaged in malaria eradication, or which have no affiliation with the international organizations sponsoring malaria eradication. Since they may represent a continuing threat of reinfection to countries that are in process of ridding themselves of malaria, a certain degree of public health co-operation may become highly desirable. Under special circumstances some synchronization of eradication activities in such contiguous countries is necessary to accomplish the common objective of eradication. Concomitant eradication activities or even the exchange of epidemiological data might be furthered through the intervention of third parties, *i.e.*, governments maintaining official relations with both.

9. INTERNATIONAL RESPONSIBILITY IN MALARIA ERADICATION

The responsibility of the participants in malaria eradication is quite different from that in most disease prevention programs; the difference is contingent upon the difference between the objectives of disease control and disease eradication. Disease control may be local or national, temporary or permanent; disease eradication must be international in orientation, and universal in application.

Successful malaria control campaigns produce temporary reductions of malaria to such low levels that, during the period of control, malaria is not "an important public health problem." These campaigns are generally limited to the more heavily populated and easily accessible malarious areas where immediate results can be had for modest expenditures of money and administrative energy. The success or failure of malaria control is a matter of local concern affecting only inhabitants of the control area. The threat of the introduction of malaria from uncontrolled areas is not important since the "controlled" area itself continues to maintain the infection.

The *annual* cost of the eradication program is considerably higher than the *annual* cost of control. But a control program continues indefinitely whereas, once eradication is achieved

within a relatively few years, the whole financial burden disappears; and the funds used become an investment in social and economic advance.

Although eradication programs are national, each country has a stake in the success of the program in every other country. Success must be global; no malarious community can be omitted. Thus eradication requires continuous nternational co-operation.

Responsibility of PAHO, WHO, and UNICEF

The governments of the Americas by actions of the XIII and XIV Pan American Sanitary Conferences in 1950 and 1954 first recommended and then instructed the Pan American Sanitary Bureau to develop the activities necessary for the greatest intensification and coordination of antimalarial work, stimulating existing programs, facilitating interchange of information and furnishing technical and, whenever possible, economic assistance to the various countries to achieve the eradication of malaria from the Western Hemisphere. The Bureau was also instructed to study international measures to insure the protection of those countries which had achieved eradication. For this purpose the Bureau was authorized to seek extra-budgetary financial contributions.

The governments of the world by resolution of the VIII World Health Assembly (1955) decided that the World Health Organization should take the initiative, provide technical advice, and increase research and coordination of resources in the implementation of a program with the objectives of world-wide eradication of malaria. The Assembly specifically authorized the Director General to obtain financial contributions for (1) research; (2) supplies and equipment . . . necessary for the effective implementation of the program in individual countries; and (3) services required in individual countries which cannot be made available by the governments of such countries.

In addition to providing technical assistance, training and research, ICA has made available a considerable part of the funds needed for imported supplies and equipment for its bilateral projects; UNICEF has done the same for malaria projects in many other countries. This has permitted PAHO and WHO to avoid very largely the direct financing of national projects and has let them devote their energies mostly to: (1) technical aid in planning and operation of the eradication service; (2) the training of personnel; (3) the coordination of national eradication services in a united regional and global eradication program; (4) the setting of standards for the organization of eradication services together with the description of operating procedures; (5) establishing specifications for insecticides, therapeutic substances, and general recommendations for cycles and dosages for application of insecticides and drugs; (6) the evaluation of the progress of national services by international experts; (7) the certification of "eradicated" zones; (8) research on special problems; and (9) the payment on temporary emergency basis of needed foreign imports and, in extreme cases, national payrolls.

The task of aiding individual countries in the development of malaria eradication programs is so great that each of the agencies concerned, the Pan American and World Health Organizations, UNICEF and ICA, has welcomed the participation of all the others in a huge co-operative effort.

So long as control and not eradication was the objective, the international health agencies could, like ICA, limit their responsibility to aiding in the purchase of supplies, insecticides, equipment and motor vehicles, and technical assistance where required.

Once the concept of malaria eradication was accepted, PAHO, WHO, UNICEF and ICA all became vitally interested in the careful planning, meticulous administration, complete coverage, continuing evaluation and coordination of malaria prevention in contiguous areas across international frontiers required for the success of each national eradication program.

The World Health Organization has a special relationship to world malaria eradication as it is through this organization that member states co-operate in the program by adapting their malaria programs to the general plan of eradication and by synchronizing their border activities with those of neighboring countries. WHO is responsible for over-all technical orientation in accord with the recommendations of its expert committees, including preparation of specifications for insecticides and pumps and the general recommendation of dosage and periodicity of application of insecticides.

PAHO and WHO can undertake the international evaluation of national eradication programs of member states without any invasion of

sovereignty and may undertake the official certification of "eradicated" areas in accord with standards already established. These agencies should constitute the clearing house for all reports of progress and of difficulties encountered; logically they are the centers for stimulating and even contracting for the research needed to solve field problems.

Responsibility of ICA

The ICA was created to further the long-term foreign policy of the United States by strengthening the economic position of the underdeveloped countries of the world. Public health projects for the control of disease at a tolerable level, where it does not materially influence the economy, have been developed as a necessary part of USOM bilateral programs in various individual countries. Malaria control projects originally organized under these programs have now entered an entirely different category. When the nations of the world decided that malaria should be eradicated from the entire world, malaria control was no longer a matter of interest solely because of its effect on the economic life of an individual country. Country projects ceased to be purely for local benefit and became units in a global campaign, of prime interest, even necessity, to all other malarious nations. When co-operation in world malaria eradication became United States policy in 1957, and ICA joined with co-operating nations in converting from control to eradication, the projects automatically became integral parts of global eradication. The antimalaria responsibility of ICA increased, as did that of each malarious country, from local efforts to reduce mortality, morbidity and economic losses due to malaria, to participation in a supreme effort to abolish malaria and to remove all future threat to the spread of infection from any country to any other country in the world.

The ICA responsibilities in malaria eradication are those assigned by the United States Government in the development and execution of its policy, plus those shared with individual governments on the basis of bilateral agreements. These responsibilities generally include joint planning, technical and administrative advice and guidance, training of national staff, and financial assistance. Unavoidably, these responsibilities entail maintaining an adequate professional maaria competence on the staff of each USOM in malarious countries.

Co-operation with international health agencies. ICA participation in national malaria *control* programs, amounting to some $13 million in 1957, represented aid to governments in alleviating the effects of malaria, at a continuing cost which would eventually have to be taken over by local governments. By contrast, the projected ICA expenditure of $38 million for 1961 malaria eradication represents the United States participation with certain governments in a capital investment of permanent value to all malarious countries. But the success of this investment depends on the development of well administered, technically sound eradication services in many of the less well developed and politically immature countries of the world. Fortunately, ICA does not have to face this burden alone; it is shared with the international health agencies. These agencies are able to operate on a wider international front than is ICA itself. By supporting the special malaria eradication funds of PAHO and WHO, ICA is able to avoid many international coordination problems and to devote itself essentially to bilateral malaria eradication projects. But even in these projects, the ICA responsibility varies with the amount of technical support which can be given by the international health agencies. It is essential, then, that ICA be thoroughly and continuously familiar with PAHO, WHO, and UNICEF malaria eradication activities.

10. TROPICAL AFRICA

In any discussion of malaria eradication, the vast area of tropical Africa, where man has lived for uncounted centuries with the tradition of malaria, merits special consideration. The intensity and continuity of transmission required to transform *falciparum* malaria into one of the most deadly scourges of mankind is guaranteed by *Anopheles gambiae*. This is undoubtedly malaria's most efficient vector, ably abetted by the almost equally dangerous *Anopheles funestus*. It is no exaggeration to state that tropical Africa, south of the Sahara, is largely populated by the remnants of a race which pays in each generation a heavy price, in illness and death, during infancy and childhood, for the apparent partial tolerance enjoyed by the adult population. That the African is not naturally immune to malignant malaria is amply documented by the outbreak in certain valleys in Ethiopia in 1958, when a prolonged rainy season permitted *Anopheles gambiae*

to breed to high densities over an unaccustomed range, resulting in some 150,000 African deaths.

There are many factors in addition to the transitional political situation which make eradication in Africa appear more difficult than in other parts of the world. Nomadism and labor migration, wide dispersal of farm plots in forest areas, prolonged seasonal, and even perennial, transmission, lack of roads and other means of transport and communication, all complicate any effort to eradicate malaria. To these difficulties must be added the poverty of the population, its high rate of illiteracy and the paucity of professionally trained persons and experienced administrators; last, but not least, is the psychological handicap of a tradition of failure in antimalaria work in Africa.

Many preventive efforts have been abortive, small scale pilot projects doomed to failure by the inexorable pressure of infection from the unprotected periphery.

Fortunately the difficulties in Africa are offset by certain advantages: (1) the very domesticity of *Anopheles gambiae* and *A. funestus*, which enhances their vectorial efficiency, favors malaria eradication by bringing these mosquitoes into intimate contact with residual insecticide on the walls of human habitations; (2) although resistance to dieldrin has been recorded for *Anopheles gambiae* in certain areas, none has been reported for DDT; (3) the tradition of failure is being broken, as in the Cameroons and in Liberia where, although early failure in total community protection was recorded, recent efforts with special emphasis on the spraying of all human habitations, farm shelters and rice kitchens, no matter how far distant from the village of the owner, have been highly successful in blocking transmission; and (4) the total population living in the rural areas of tropical Africa is comparatively small; although the per capita cost may be high, the cost *per* continent ought not to be excessive.

The wave of independence now sweeping Africa with the sudden emergence of new nations, inexperienced in national administration, must inevitably produce, in some cases, administrative chaos. Such chaos should be temporary, and as stability develops, the new African governments should become sensitive to the health needs of their peoples. No doubt the new nations in Africa will see DDT more generally used, often as a tool for gaining political prestige; the eradicationist should be on hand to take full advantage of this developing situation rather than be forced, as in other parts of the world, to build *malaria eradication* on the failure of malaria *control* to give adequate long-term protection.

The political leaders of Africa's new nations are well informed of the drive to eradicate malaria from the rest of the world and African resentment has been openly expressed in the World Health Assembly with the idea that malaria eradication in Africa can wait until other continents and other races have been freed.

It is important in Africa, because of the intensity and universality of malaria transmission and the extensive movement of peoples within countries and across national frontiers, that antimalaria activities be carefully planned and that each national plan be coordinated with those of neighboring states.

Inevitably this means that bilateral malaria programs in which ICA may be participating will depend for their ultimate success on work done in neighboring states. ICA must work most closely with WHO in planning and developing eradication projects in Africa, and these should be grouped where possible as an area or regional program.

The Panel believes that the present modus operandi, with the ICA and WHO approaching governments individually to develop national projects, does not meet the African situation adequately. The Panel recommends that ICA study the malaria problem of tropical Africa as a whole and co-operate intimately with the WHO in the development of a regional program.

Malaria eradication, more than any other activity, can set the pattern for international co-operation of the African nations in the solution of common problems.

Malaria eradication is the key to the solution of Africa's major problems in education, agriculture, industry and transportation, and of its other diseases, and poverty. While malaria is important in many other regions of the world, in Africa the solution of this problem is fundamental to all progress.

11. SOCIAL IMPLICATIONS OF MALARIA ERADICATION

Socioeconomic Effects

The Panel appreciates the purely economic benefits of malaria eradication but believes that the intrinsic value of human life and health is paramount.

Some older members of the Panel who have observed man's degradation by malaria and his ineffectual struggle against it in the pre-DDT era have revisited, in recent years, such formerly malarious areas as the Southeastern States of the United States, Sardinia, South Italy, India, Taiwan and Thailand. They have been impressed by the obvious beneficial transformation of the life of the people. It seems apparent that liberation from malaria is the prime reason for this change. Malaria eradication, however, is rarely given full credit for the benefits it brings; rather, the latter tend to be attributed to the increased population which crowds into the area to take up agricultural lands previously unattractive, to the introduction of industry, to the improvement of schools and of roads, and to many other previously impossible developments.

Sometimes one is so close to events of great social, cultural, and economic impact that perspective is lost; in the case of malaria eradication, no one can visualize its total effect on the future of mankind, especially in the tropics.

India has been sometimes thought of as an exhausted country with hundreds of millions eking out an existence through marginal agriculture; in fact, India is a rich country. Malaria, more than any other disease, has contributed to its poverty.

The following quotations are pertinent:

"The most important tropical disease in India is malaria. After allowance is made for the tendency to attribute to fever, deaths from other causes, malaria stands out as universally prevalent in India, and in many tracts it is a greater scourge than either plague or cholera. It maims as well as it kills, and causes more sickness, misery and death than any other single disease." (Resolution of the Government of India, Department of Education, 1914.)

"Whether from the point of view of enhanced mortality, sickness and individual suffering, or from the effect of preventing natural increase and sapping the vitality of populations, or the paralysing effect on industry and exploitation of the mineral or other natural wealth of the country, or in the direct loss to Government in a variety of ways, malaria is universally recognized as the most important sanitary problem with which India has to cope." (Christophers, 1926.)

"The problem of existence in very many parts of India is the problem of malaria. There is no aspect of life in this country which is not affected, either directly or indirectly, by this disease. It constitutes one of the most important causes of economic misfortune, engendering poverty, diminishing the quantity and the quality of the food supply, lowering the physical and intellectual standards of the nation, and hampering increased prosperity and economic progress in every way." (Sinton, 1936.)

Those who have visited India recently realize that this is becoming in large part a story of the past, in sharp contrast to the present. With the enormous progress in malaria eradication, a new era is opening.

Money spent on eradication is not only an investment in social progress, but has proved to be a sound investment in economic development. Since data on this latter subject are fragmentary, the Panel suggests that it would be advantageous for ICA to solicit the aid of economists to study the effect of eradication on the general economy of the areas concerned, including the effect on agriculture, power development, industry and tourism, as well as the effect on education.

Malaria and Population Growth

Malaria, especially in hyperendemic areas, whether in the tropics or in the temperate zone, is notorious for its effect on population growth; this effect occurs not only through excessive mortality but also because of reduction in fecundity. Many areas of the world have resisted repeated attempts at colonization because of the failure of settlers to maintain a stable population.

Malaria prevention not only reduces human suffering from malaria but diminishes the number of untimely deaths and permits the establishment of normal positive birth/death ratios. Thus the prevention of malaria, as the prevention of other communicable diseases, tends to be followed, other circumstances aside, by an accelerated growth in population. But in those areas where malaria is hyperendemic, conditions are radically changed when malaria is prevented. A population free of malaria has possibilities of productive labor and of effective education and training undreamed of in hyperendemic areas.

The predicted effects of uncontrolled population expansion upon subsistence resources, national economies, and even on world peace, have been viewed with portentous alarm by those who lack faith in the operation of normal biological balances in the case of the human race. For the record it should be stated that, on the basis of economic and social conditions existing in the

United States thirty-five years ago, it was confidently predicted that the population of this country would grow much more slowly than has been the case during the past twenty years; that it would reach an equilibrium, forced by natural limitations of agricultural and other resources, when the population became one hundred seventy-five to one hundred eighty million souls. This level has been reached together with excess production of foodstuffs and with no immediate cause for alarm generally recognized.

The situations in different parts of the world vary widely; some areas will be ready and able to use the additional productive capacity and increased numbers of population as they are freed from malaria; other areas, as they are freed, may find great difficulty in doing so within a short period. In the latter condition, it has been argued that the normal biological control in the human race, based on a balance between natural resources, number of population and living standards acceptable to the population, will operate too slowly to avoid disaster. Many insist that a significant effort should be made to bring about and maintain a compensatory balance between natality and mortality through education of the public on the advantages to be gained from limiting the size of family in accord with its economic and social situation.

There is also the fact that size of total population is only one side of the equation—the other side being the amount of production, distribution and consumption of goods and services. Proponents of this point of view insist that education and training, plus investment in productive enterprises, will add to the other side of the population–consumption equation.

In any event education is not feasible nor production of goods and services possible where the population is stricken with disease. Malaria eradication is a start toward breaking out of the vicious circle of disease-ignorance-poverty-disease-ignorance-poverty.

12. FINDINGS AND RECOMMENDATIONS

Findings

Malaria eradication is feasible. Evidence has accumulated since the malaria eradication program was launched, firmly supporting the feasibility of world-wide malaria eradication. It is obvious that global eradication must come about as the cumulative result of successful nation-wide eradication programs in all malarious countries; successful malaria control programs, limited to the more heavily populated, economically important areas of a country fail to promote the mutual long-range interests of all malarious countries.

The principal method of achieving eradication continues to be the application of residual insecticide to habitations to destroy the vector—a house-frequenting mosquito—and thus prevent transmission of the malaria parasites. In situations where the habits of the vector or the living conditions of the people at risk make residual insecticiding ineffective, alternate methods may be required. These include larviciding, elimination of breeding places, and the use of antimalarial drugs. To achieve eradication it is essential that there be (1) a complete geographic delineation of all malarious areas; (2) a total attack on malaria transmission in such areas; and (3) thorough surveillance to appraise results and to prevent reinfection.

A number of technical problems have appeared which complicate malaria eradication. These include insecticide resistance of the mosquito vector, drug resistance of the malaria parasite, variability and modification in the type and construction of dwelling to be sprayed, nomadism and mass population movement, and unusual habits of the mosquito vector. Experience shows that early and continuing epidemiological evaluation and entomological research are required to recognize and solve these problems where they exist.

Resistance of mosquito vectors to insecticides used in residual spraying continues to complicate eradication programs. The number of vector species resistant to DDT or dieldrin has steadily increased and as of early 1960 comprised 21 species (1 to DDT alone, 13 to dieldrin alone and 7 to both DDT and dieldrin), present in areas of at least 29 countries. The resistance problem is intensified by the widespread use of insecticides for agricultural purposes and is certain to become more acute the longer these insecticides are used. Other insecticides such as malathion, to which resistance has not yet appeared, can be used in eradication but their employment will be more costly. Every effort should be made to initiate effective eradication programs in all areas as soon as practicable to make the most rapid progress while there is still minimal resistance to DDT. Careful study of mosquito popula-

tions is necessary to detect the onset of resistance and intensified research must be aimed at the development of cheap, safe, substitute insecticides effective against resistant mosquitoes. In evaluating the over-all significance of the resistance problem, the Panel members are confident that this is not now an insurmountable obstacle to malaria eradication and that adequate research will provide the means for achieving the final objective.

Resistance of the parasites to antimalarial drugs has appeared in widely scattered areas of the world. In general, the phenomenon is sporadic and limited to proguanil and pyrimethamine. (After this report had been submitted, evidence appeared that certain strains of plasmodia may become resistant to chloroquine.) Fortunately, parasites resistant to these drugs currently respond well to other agents such as chloroquine and amodiaquin. The Panel believes the use of drugs will continue to be an important adjunct to programs of malaria eradication.

Continued research is needed to produce a drug with prolonged preventive action, preferably up to six months, and to solve the problem of drug resistance.

Eradication of malaria in any large area may be nullified by the reintroduction of the parasite. To minimize this danger there should be total coverage over entire areas of epidemiological equivalence, as though political boundaries did not exist, and within which infected individuals move freely. Especially acute problems of this sort occur where nomadism exists.

As has been demonstrated in many geographic areas, malaria eradication can be achieved in 8 years or less. Programs are normally 1 year of administrative preparation, including surveys, 4 years of spraying and 3 years of surveillance. Experience has shown that social and economic benefits will be evident after the first or second year of spraying. It should be recognized, however, that in certain countries, because of administrative, financial or technical difficulties country-wide eradication may require a longer period. Popular and governmental support, quite substantial during the early phase of eradication when dramatic reduction in malaria occurs, has been difficult to maintain for the essential final work in peripheral populations and isolated foci.

At present there is ambiguity as to the standard dosage for residual insecticide and the minimal frequency of application. The recommendations of the WHO Expert Committee frequently have been interpreted as indicating that 2 grams per square meter (2 g/m^2) of technical DDT should be applied every 6 months, or 0.6 g/m^2 of dieldrin every 12 months. On the basis of recent laboratory data and field experience, it is apparent that a *standard* treatment of 1 g/m^2 of DDT every 6 months is adequate unless entomological and epidemiological studies show that under local conditions other dosage, other insecticide or other schedule of application is indicated. In case of DDT resistance, 0.25 g/m^2 of dieldrin, every 6 months, should be adequate provided that resistance to dieldrin does not exist. In the case of resistance to both DDT and dieldrin, malathion is recommended as a substitute. Dosages of malathion have not been established, except on mud walls, where 1 g/m^2 every three months is recommended.

It is important that epidemiological and entomological studies be instituted in each country along with spraying operations to obtain information essential for the effective and efficient use of insecticide.

Progress. The results of the world-wide malaria eradication campaign to date are encouraging. As must be expected in a world of almost infinitely varied forms and degrees of social, economic and cultural development, and of political stability, progress of malaria eradication has not been equal throughout. There have been exaggerated expectations in some quarters stemming from lack of understanding of the technology involved, and even more so of the political, administrative and financial arrangements required for successful application of that technology. In general, progress toward the elimination of malaria, globally, since the world-wide program was launched, despite the human, physical and technical obstacles, is truly gratifying, and fully justifies the expectation that the world-wide goal, unique in public health history, will be achieved.

It seems evident that in certain countries eradication will be accomplished, or virtually accomplished, within a period of 5 or 6 years from the date of the initiation of, or conversion of control programs to, eradication.

In the light of eradication experience in many countries, an arbitrary "standard" 8-year program has been adopted, longer than the minimal time required in some nations, perhaps not long

enough in some others offering unusual obstacles. Eradication programs are only now being started in some malarious countries, or have yet to be initiated in others, particularly in some of the evolving nations of Africa. But it must be emphasized that malariologists have been surprised at the accelerated development of programs, once the concept of eradication has seized the imagination of the peoples concerned.

The response to the call by WHO in 1955 for global eradication has been even more enthusiastic in malarious countries than had been anticipated. The number of countries and territories in various stages of the campaign rose from 60 in 1956 to 95 in 1959.

The time has been too short for any of the campaigns to be completed, but the numbers of persons under protection by spraying has risen to the astonishing total of over 500 million. This is incomparably the greatest single public health program of all time.

The dramatic reductions in death and illness from malaria (frequently more than 50% after the first year of complete coverage by spraying) have made the campaigns generally popular and have laid the foundation for basic economic improvement.

Through the malaria eradication program, government has, in many areas, for the first time established public health contact with tens of millions of persons, mostly in rural villages. In response to the awakened popular demand created by this contact, government is in some of these areas beginning to take other practical steps to improve health. Public health work tends to snowball under popular pressure; this popular pressure itself is a force to impel government to complete malaria eradication.

Experience shows that vigorous public health education to convince the individual that he and his family do not have to have malaria and to enlist his active participation greatly facilitates malaria eradication.

Obstacles to progress. The chief obstacles to progress in malaria eradication are:

(1) *Failure to approve adequate financing.* Before a project is initiated, adequate financing for the whole program should be agreed upon in principle and funds allocated each year well in advance to prevent the possibility of a shortage of funds delaying or interrupting operations. Failure to do this has been almost ruinous to some eradication projects.

(2) *Weakness of administrative structure.* Many health ministries are slow in making the major adjustments needed for a successful malaria eradication campaign. Creation of a semi-autonomous body is strongly recommended; this requires negotiation and new legislation.

(3) *Shortage of trained manpower.* This problem is well-nigh universal. It calls for special training courses organized a year or more in advance and for competent personnel to be made available promptly for the course. Especially important is the training of administrators—not only for supply, transport and finance—but also for the wider functions of public health administration. For most malarious countries, these men must be trained abroad. Pending their preparation, the country must depend on international cooperation for the supply of such key personnel.

(4) *Shortage of specialists.* This applies to all categories generally, but, in the United States, especially to medical public health administrators and epidemiologists trained in malaria eradication. Suitable courses for the training of these specialists are not now offered by any university or school of public health in the United States.

(5) *Lack of basic epidemiological data.* In many countries, considerable time, often a full year, must be devoted to the collection of basic information, including the preparation of a "malaria map" delineating the malarious areas and a census of human habitations with estimates of the extent and kind of wall surfaces to be found.

(6) *Inadequacy of reporting.* In many projects, spraying operations and evaluation have been instituted without proper provision for detailed reports of what is occurring at a given place at a specified time. Reporting must be improved to permit of continuing analysis of progress on which corrective action can be based.

(7) *Shortage of international (PAHO/WHO) teams of epidemiologists.* These teams are invaluable for checking national projects and facilitating an interchange of current experience. Unfortunately, they have not always been available when needed.

Duration. The Panel is unable to suggest a terminal date for global eradication because:

(1) A malaria control program does not become one of eradication merely by changing its name, but only by reorganization to the rigid specifications of eradication. The standard 8-year period may not be adequate unless the whole area is brought under spraying promptly with

no major errors and no important interruption in operation, and without encountering any major technical obstacle.

(2) Although the number of countries and territories that have announced a policy of malaria eradication has risen since 1956 from 60 to 95, some of these are not yet fully operational.

(3) Many other countries still have pilot studies underway, upon which final plans must be based. The duration of such studies cannot be predicted with any degree of accuracy.

(4) Estimates of population in malarious countries where eradication has not yet begun are probably inaccurate. Experience has shown that the population to be covered in certain countries conducting eradication projects has been greatly increased by the inclusion of large numbers of people in areas only lightly malarious. In India, alone, for example, these numbers run into more than 150 million.

(5) Problems of resistance are increasing. Although these are not insurmountable, they may lengthen the duration of the campaigns in the countries involved.

(6) Local financing may fail. Unless external funds are promptly available, operational breakdowns will inevitably lengthen certain programs.

Cost. WHO estimated that world-wide eradication of malaria would cost $1.7 billion from calendar year 1959 to its completion. This figure includes estimates for the Communist countries (including China), and Africa and the cost of three years of surveillance for all programs, at an annual rate ranging from 40 to 75% of the annual cost of spraying.

On the basis of information presently available from WHO, PAHO, ICA, UNICEF, and other sources, the Panel estimates that for the period beginning with calendar year 1960, the cost of eradicating malaria in *the free world* will not be less than $1.3 billion, of which $390 million would be foreign exchange cost and the equivalent of $950 million would be local currency cost.

The above estimates of minimum cost are in terms of dollars of present purchasing power and of basic procedures currently followed in the conduct of the eradication programs. They do not allow for technical and administrative contingencies or improvements which experience suggests will occur. Not less than 50% in the case of total cost, and not less than 25% in the case of foreign exchange cost, should be permitted as an adequate safety factor in such long term estimates. Annual revision of estimates on the basis of additional experience is essential.

Recommendations

The Expert Panel on Malaria has expressed points of view and opinions and made suggestions and recommendations throughout the body of this report. The principal recommendations of the Panel are that:

(1) United States support of world-wide malaria eradication, a program accepted and approved by the nations of the world at the World Health Assembly in 1955, continue until the objective is achieved;

(2) the United States consider support for additional country eradication projects in response to the clear initiative of national governments, especially in countries with large populations such as Pakistan, and giving preference to countries adjacent to those where eradication projects are in progress;

(3) the total level of malaria eradication financing from all sources not be permitted to decline until a large number of countries pass from the attack phase into surveillance and beyond;

(4) the United States make efforts to obtain substantially larger contributions to the Malaria Eradication Special Accounts of PAHO and WHO from the member governments of economically advanced countries; meanwhile, the United States maintain its contributions to the Special Accounts at adequate levels; encouragement be given to countries which have eradicated malaria to assist in the remainder of the global campaign;

(5) the United States give separate consideration to tropical Africa; ICA cooperate intimately with WHO in planning eradication for Africa as a single program; the United States take the initiative, *without prejudicing malaria eradication elsewhere*, possibly by creating an African Malaria Fund, and seek the participation of other nations;

(6) ICA provide funds for expanded research in epidemiology, surveillance, entomology, insect resistance, dosage and cycle of application of insecticide, chemotherapy, persistent fumigants, and such other problems as may emerge in the course of eradication;

(7) ICA encourage the recruitment of medical public health administrators and epidemiologists

and provide for their training in malaria eradication, by subsidizing suitable courses in schools of public health in the United States;

(8) ICA insist on early and continuing epidemiological evaluation of eradication projects in which it participates and be prepared to withdraw its support from projects where failure to register reasonable progress can be attributed to the lack of government support or inadequacy of administrative controls.

Administrative Principles in Malaria Eradication Programs

It is recommended that all ICA-aided malaria eradication programs, whether new or continuing, obtain acceptance of the following administrative principles:

(1) The Director of a National Malaria Eradication Program has the prime responsibility for seeing that malaria is eradicated in his country. To do this, he should have full administrative authority, that is, effective control of nationally budgeted malaria eradication funds and of resources made available for the program, and also, control of personnel, including hiring and firing. Care must be taken in the selection of a Director competent to exercise this authority.

(2) Malaria eradication programs require dedicated leadership and strong organizing ability. A vigorous sense of responsibility and discipline is essential in the Director of malaria eradication programs. He should have the judgment and ability to delegate authority and to command respect. He should be strong in dealing with inefficiency.

(3) The enforcement of these principles should be delegated by the Director to all levels of supervision in his organization, down to the lowest supervisory echelon.

(4) It should be emphasized that responsibilities are assigned not only for operation, but primarily, for results; responsibility is not discharged by spraying a certain number of houses, but by interrupting malaria transmission.

(5) In malaria eradication programs, the area of activity should be divided into geographic units, each under an individual who has *complete responsibility* for the accomplishment of malaria eradication within his area.

(6) Experience has proved that success in eradicating malaria depends in large measure on adequate supervision and checking of assigned tasks. Great emphasis must be placed on this point. Employees should be taught to expect thorough checking of assigned tasks and inevitable disciplinary action for failure or neglect in discharging their assigned duties.

(7) Experience in eradication programs has proved that when these administrative principles and procedures were followed, success was certain. Experience has also demonstrated that when these principles have been neglected or ignored, eradication programs have suffered serious delay with increased costs and threatened failure.

ANNEX I: COUNTRIES WITH ICA MALARIA ERADICATION PROJECTS

Far East
- Cambodia
- Indonesia
- Laos
- Philippines
- Taiwan
- Thailand
- Vietnam

Near East and South Asia
- Ceylon
- India
- Iran
- Jordan
- Nepal

Africa
- Ethiopia
- Liberia
- Libya

Latin America
- Bolivia
- Brazil
- Colombia
- Ecuador
- Guatemala
- Honduras
- Jamaica
- Nicaragua
- Paraguay

ANNEX II: EXAMPLES OF MALARIA ERADICATION

While malaria eradication means the ultimate elimination of the parasite of malaria from the world, this ultimate objective must be reached by stages. In planning the program of malaria eradication, it is justifiable to speak of local, insular, provincial, national, regional and global eradication as parts of a continuing development. It is obvious that all "eradicated" areas, until the ultimate is reached, are threatened by reinfection and each eradicated area must be protected by continuing expansion of "eradication," first from contiguous areas from which reinfection could most easily come, and eventually from the last existing focus in the world.

The examples presented have been chosen for their historical interest or because of specific lessons to be learned.

Sardinia (Insular Eradication)

The first cycle of island-wide spraying of human habitations with DDT was carried out from November 1946 to June 1947. Since the program in Sardinia was planned for the eradication of *Anopheles labranchiae*, larviciding was also practiced in later years. Reduction in reported malaria was dramatic (Table 7).

There is no evidence of malaria transmission in Sardinia since 1950 although a few imported cases have been seen and a few infections contracted through blood transfusions. An observer reports in 1958:

"The disappearance of malaria has brought about great changes in Sardinia. The general health of the people has noticeably improved and the output of work has increased. Large-scale land transformation projects are in progress in the country, and regions formerly uninhabited, or uncultivated, are now built up with houses and, in some cases, villages have appeared, as for example, in the Nurra, the lower Tirso Valley, Guista (south of Oristano), Uras, Castiadas, Orosei, Ozieri, etc.; frequently one feels one is in the Agro Pontino."

TABLE 7

Cases of malaria reported by provincial medical officers in Sardinia from 1946 to 1950

	Before DDT 1946	After DDT			
		1947	1948	1949	1950
New cases	10,149	2,968	341	6	4
Total cases	75,447	39,303	15,121	1,314	44

TABLE 8

Illness and deaths attributed to malaria in the Province of Latina

	1944*	1945†	1946‡	1947	1948	1949
New cases	35,969	2,382	96	6	0	0
Total cases	54,929	44,712	30,929	6,456	1,327	97
Deaths	120	160	19	0	0	0

* Reports for 1944 cover only the second half of the year following the withdrawal of the German Army.

† In 1945, control measures using Paris green as a larvicide.

‡ In 1946, the first year application of DDT.

Italy (Provincial and National Eradication)

The following quotations are from a recent publication, "A Great Social Achievement: The Eradication of Malaria in Italy." (E. Mosna, *Riv. parassit.*, **20**: 335–336, 1959.)

"From the results of two antianopheline campaigns conducted in Italy in 1945 (one by Missiroli and co-workers in the "Paludi Pontine", and the other by Soper and co-workers in the "Agro Romano") it could be concluded that in the Mediterranean area, in which malaria is due in great part to anophelines of the *A. maculipennis* group, adulticide measures were sufficient to interrupt the transmission of malaria whatsoever were the housing conditions.

"Following Missiroli's five-year antimalarial plan for Italy proposed in January 1946, operations for the eradication of malaria in the Province of Latina were initiated in March of the same year, in order to obtain new practical criteria for the future organization of the antimalarial campaign in the whole of Italy. . . .

"Anti-adult operations with DDT were carried out annually from 1946 to 1953: the internal walls of all human dwellings and animal quarters in the malarious zone of the Province were sprayed. A vigorous surveillance on residual anophelism was maintained thence. . . .

"Anti-adult measures with DDT have brought about eradication of malaria (*P. falciparum* in the third year and *P. vivax* in the fourth year of the campaign).

"As regards the malaria vectors, through treatment with DDT *A. sacharovi* has disappeared from the Province after 2 years and *A. labranchiae* after 4 years of the campaign.

"The rapidity of the disappearance of malaria in the Province of Latina was indeed heartening and gave strong support for the proposal for national eradication in all Italy. [Table 8.]

"For the ten years, 1950 through 1959, no cases of malaria nor deaths from malaria were reported from this previously heavily malarious province.

"In the other provinces of Italy in which there were zones considered malarious (with exception of Sardinia, where it was tried to achieve eradication of anophelines), the anti-adult measures with DDT, started nearly all in spring 1947, following the procedures used at Latina, have practically led to disappearance of malaria after 5 years. After so many centuries

of the ravages of malaria, already in 1948, i.e., only two years after the start of the DDT anti-adult campaign, no case of death due to malaria was reported in Italy."

While the results for Italy as a whole have not been as absolute as those from Latina, they give dramatic proof of the rapidity with which malaria infection disappears once transmission stops. In 1946, 374,163 cases of malaria with 280 deaths were reported in Italy. No deaths have been reported since 1949, and less than 100 cases in any year after 1952. Until sources of reinfection have been eliminated, Italy may continue to have occasional localized epidemics, as in a rural center in Sicily, 1956, when some 78 new cases were observed. Italy has no recognized malaria problem continuing year after year.

Taiwan (Insular Eradication, Terminal Stage)

The experience in malaria control and eradication in Taiwan is most instructive. A study of this experience indicates that careful current epidemiological evaluation with continuing adaptation of operations to needs, may, under favorable conditions, lead to eradication of malaria at a lower cost than estimated on the basis of the standard eradication procedure.

Taiwan has been recognized as a highly malarious area ever since the Japanese invasion of 1896 when 6,000 troops suffered 16,000 infections in a single year. The Japanese program of quinine distribution and obligatory treatment of cases broke down during World War II and malaria became rampant throughout the Island. The Rockefeller Foundation collaborated with the government in 1946 in creating a Malaria Institute for the training of malaria specialists and for studying malaria and its vectors. In 1951, when estimated cases of malaria reached 1,200,000, with 11,000 deaths, the health authorities began plans with the collaboration of ICA and of WHO, for an island-wide *malaria control* program.

The control program began officially in May 1952, with operations that year limited to studies and to preliminary testing of methods; in 1953 house spraying was carried out in the most malarious parts of the island; in 1954 control was extended to a much larger area of median malaria intensity; in 1955 spraying also covered the small population living in the foothills and mountains.

Late in 1955, animated by the declaration of the World Health Assembly for malaria eradication and spurred on by the obvious results of the work already done in Taiwan, the authorities decided to transform the control service to one for the *total eradication of malaria.* In 1956, the rest of the island was sprayed except for purely urban areas, the only permanently malaria-free parts of Taiwan.

In the readily accessible heavily populated areas, spraying with DDT resulted in the disappearance of malaria transmission and of most of the cases within a two-year period, and in many areas in the almost total disappearance of the principal vector, *Anopheles minimus.* The malaria situation was such in 1956 that spraying was cut back in 1957 to the heavily malarious area covered in the first year's spraying (1953).

A survey made in 1957 indicated that most of the Island of Taiwan was free of malaria transmission; that there were some eight residual foci of transmission which could be differentiated as (1) four foci where house spraying had never been carried out and (2) another four foci where low-grade transmission occurred in spite of previous spraying.

In 1958, house spraying was limited to the population of these eight residual foci and that of surrounding and contiguous areas. Active surveillance on an intensive scale was established for this population with drug treatment for all infected persons found. A less rigorous and more economical surveillance was established for the rest of Taiwan's population.

Table 9 shows how far the Taiwan program has varied from the standard "planning and costing" eradication program of one year of preparation, four years of complete house spraying followed by three years of complete uniform surveillance to determine that eradication has occurred. The table also shows that the cost of undertaking eradication, a decision taken late in 1955, had largely been underwritten by the previously organized control campaign, the peak year of expenditures having been 1954! The total per capita cost of eradication projected to the end of 1961 is $0.82 U. S. A. of which $0.57 had been spent by the end of *1955.*

In considering the Taiwan program attention should be given to certain deviations from the standard WHO eradication program of one year of preparation, four years of spraying and three

TABLE 9

Development by years of malaria control and eradication program in Taiwan, 1952 to 1961

	Estimated population (in thousands)									
	1952	1953	1954	1955	1956	1957	1958	1959	1960	(Estimate) 1961
Total for Taiwan	8000	8250	8500	8750	9000	9270	9630	10000	10600	11000
In malarious areas	6750	6986	7200	7460	7710	8000	8280	8560	8830	9140
Attack phase	156	1500	5500	5650	6728	1470	310	260	100	0
Consolidation phase	—				0	1300	2720	2430	2500	1700
Maintenance phase	—				982	5230	5250	5870	6230	7440
Costs (US$)										
Annual expenditure	186,680	773,770	1,889,400	1,246,270	943,070	238,315	160,759	270,879	259,041	169,670
Per capita—for population at risk*	.03	.11	.26	.17	.12	.03	.02	.03	.03	.02

* The per capita costs include in the year of expenditure the costs of "tooling up" which are not amortized under the life expectancy of the equipment. Costs of equipment are likewise included in the year of purchase. In an eradication program in which every step of the program is for the permanent protection of the total population at risk, all costs should be charged against the total population to be permanently protected without consideration of the percentage of the population to which a given measure is being applied in a given year.

of surveillance. Not all of the malarious areas in Taiwan were sprayed the same length of time.

In 1957 only the heavily malarious area with 1,500,000 population where spraying began in 1953 was sprayed; in 1958 this was reduced to 300,000 living in potentially infective areas, in 1959 to 260,000 and in 1960 to 100,000. The *amount of spraying done in Taiwan added up to about three years spraying for the population living in the malarious area.* It should be noted that the spraying in Taiwan consisted of a single annual application of DDT at the rate of 2 g/m^2.

It should be noted also that there has not been blind obedience to the formula for the application of surveillance on the same scale throughout all of the previously malarious areas. Surveillance has been very intensive in residual foci of infection and in potentially malarious areas with considerable insistence on mass blood parasite surveys, but this intensive study has been concentrated in only a few hundred thousand of the population previously at risk.

To summarize, one can say that the use of epidemiological information at all stages of the Taiwan program to orient both spraying and surveillance activities has speeded up the program of eradication and greatly reduced the over-all costs. (There can be little doubt that Taiwan is on the verge of eradication, only 167 persons having been identified as carriers of plasmodia during 1959 when some 775,000 blood slides were examined in an intensive search for malaria parasites.)

TABLE 10

Year	"Eradicated" area (sq km)	Percentage of increase
1951	131,954	0.0
1952	156,938	18.9
1953	199,740	27.3
1954	248,701	24.5
1955	305,414	22.8
1956	361,045	18.2
1957	372,601	3.2
1958	400,414	7.5

Venezuela

In any history of malaria eradication in the Western Hemisphere considerable attention must be paid to the development of the program for the eradication of malaria in Venezuela. Not only is Venezuela the meeting place for various species of malaria vectors having quite different breeding and feeding habits, but it also lies entirely within the tropics and is the first tropical country in which a nation-wide program for the eradication of malaria was planned.

"The nation-wide campaign against malaria in this country, begun in 1945, was based on DDT indoor residual spraying and has as its aim 'the eradication of malaria from Venezuela' by 'protecting all the houses of the malaria zone, even those of sparsely populated or mild districts' . . . The initial plan contemplated having the whole country malaria free by 1955, after spraying 100% of the houses of the infected zone."

The Venezuelan experience has been most important, especially because of some of the difficulties encountered. A point of major importance which should be taken to heart by workers in other countries is the Venezuelan experience indicating that the smallest political divisions, the municipios, or counties, are the most appropriate units for the study of progress towards eradication.

A single indigenous case found in any county was sufficient to keep that county in the infected area. Measuring the results of operations by counties called attention to the particular counties in which there were problems to be resolved, whether these problems were administrative or epidemiological. By 1951 there was an already considerable area which during three years had not been known to have any indigenous cases. The annual increase of the malaria "eradicated" area of Venezuela is shown in Table 10.

In 1959 the territory still infected in Venezuela "is formed by 59 municipios with an area of 155,874 square kilometers and a population of 520,000 inhabitants." Not all of these inhabitants live in localities where malaria transmission still occurs. A study of the number and distribution of cases occurring in 1958 has led to the following statement: "These figures indicate that malaria is reaching the vanishing point in Venezuela and that if the work with drugs (pyrimethamine and primaquine) is finally successful Venezuela may still be the first continental country in the tropical zone to become entirely free of malaria."

Venezuela and British Guiana which began eradication in the same year both registered rapid and easy conquest of malaria in those areas where malaria transmission was very heavy and where the vector *Anopheles darlingi* was so highly domestic that it disappeared rapidly from the areas in which all of the human habitations were sprayed with DDT. Venezuela has long been free of malaria in all those areas in which *Anopheles darlingi* was the principal vector but still has difficulties in the areas infected with *Anopheles aquasalis* and *Anopheles nuñez-tovari*, vectors whose behavior is quite different from that of the more efficient *Anopheles darlingi*.

Added to its other difficulties Venezuela has suffered rather constantly from the introduction of malaria infection from neighboring countries, particularly across land frontiers.